

Figure 1

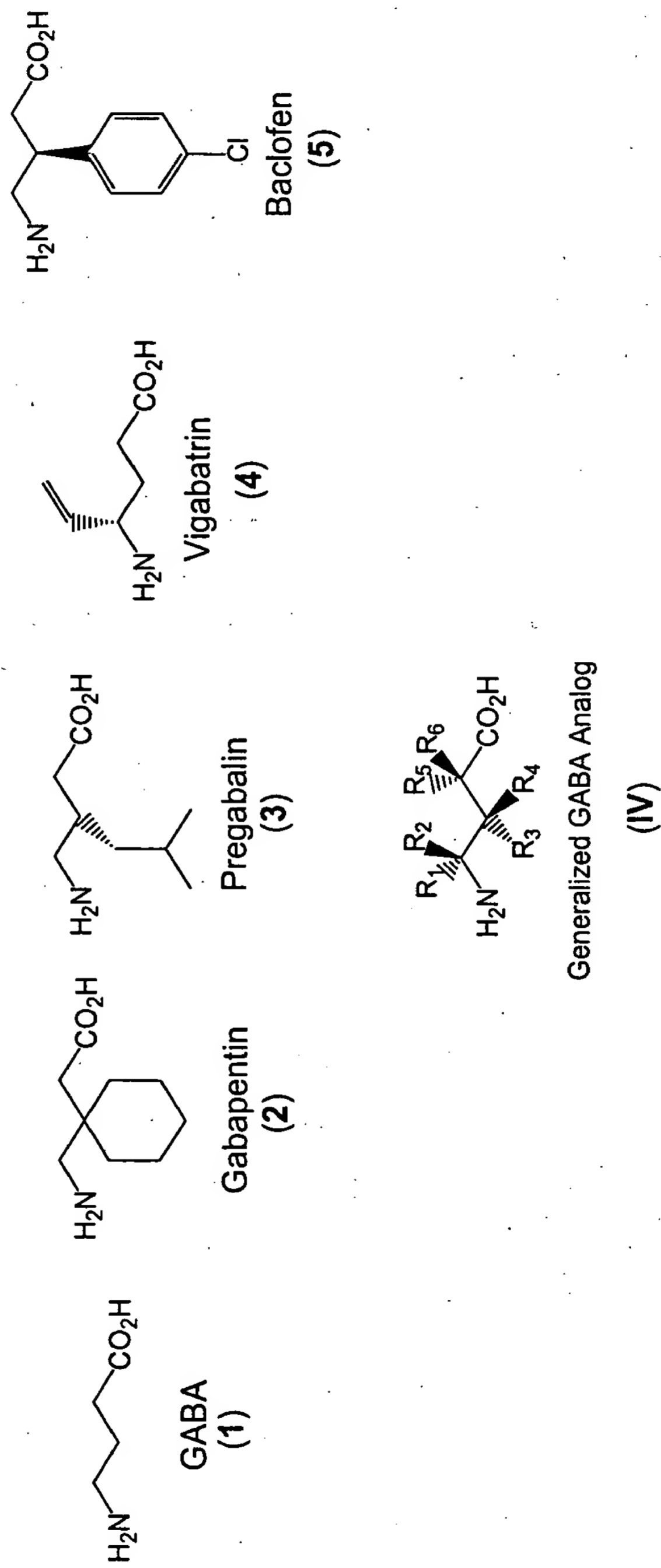


Figure 2

The Enterohepatic Circulation with Key Transporter Proteins Mediating

Bile Acid Circulation

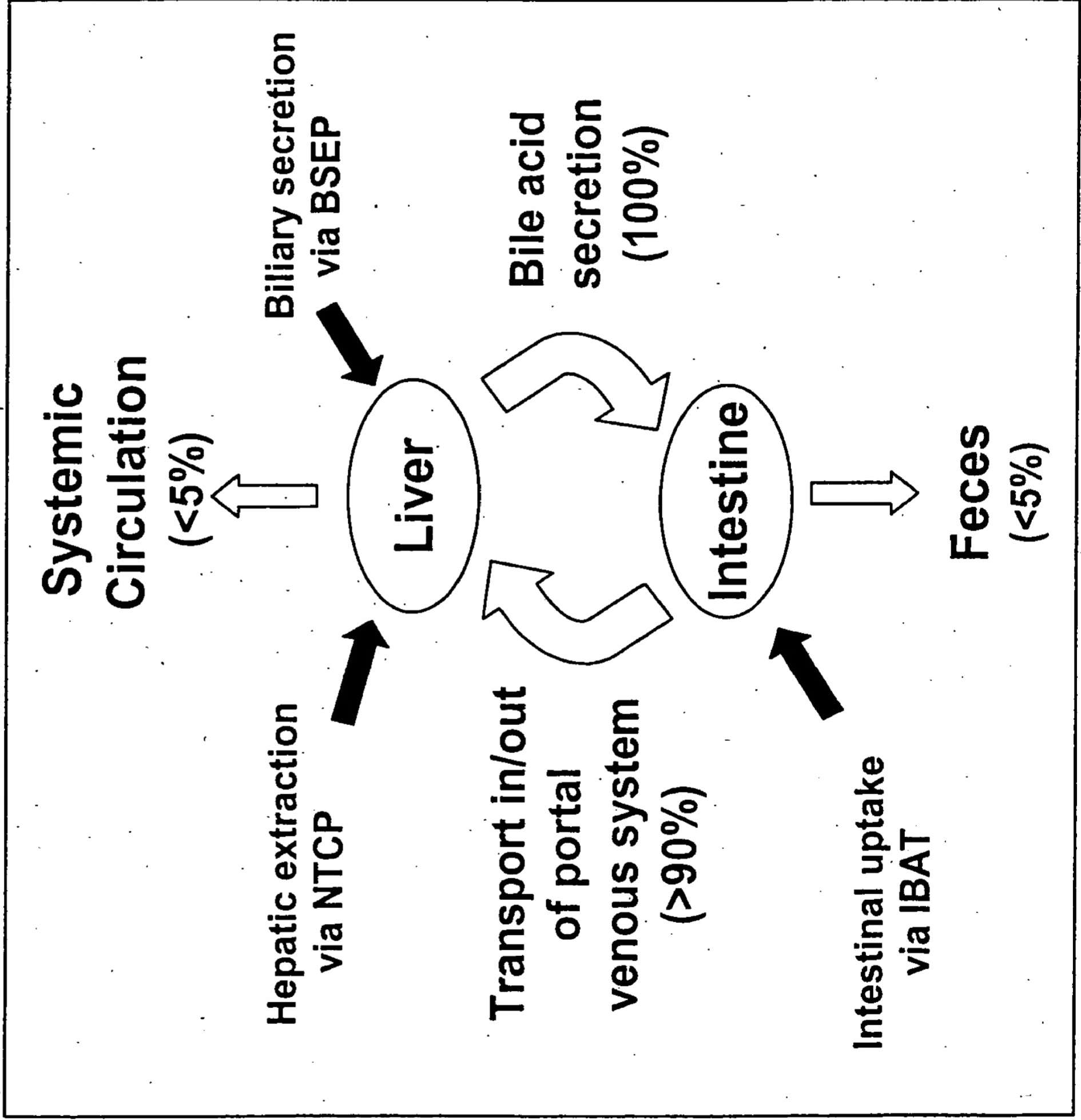
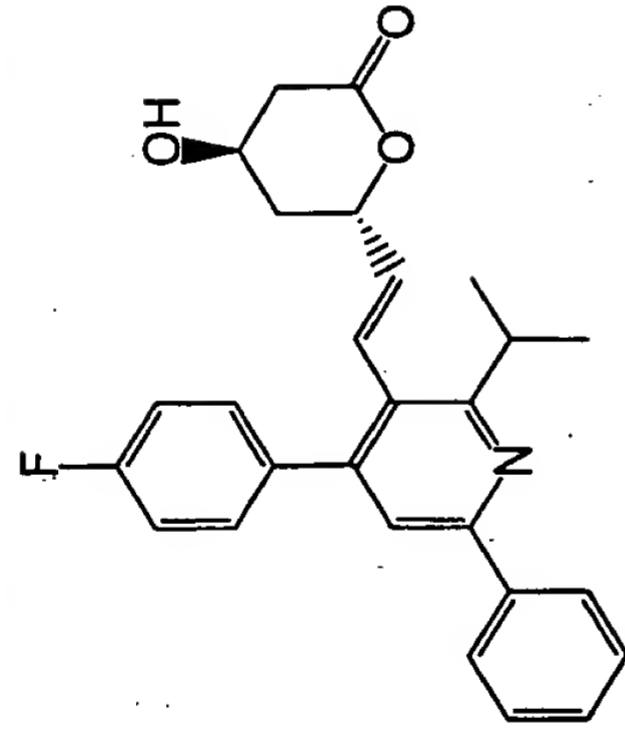
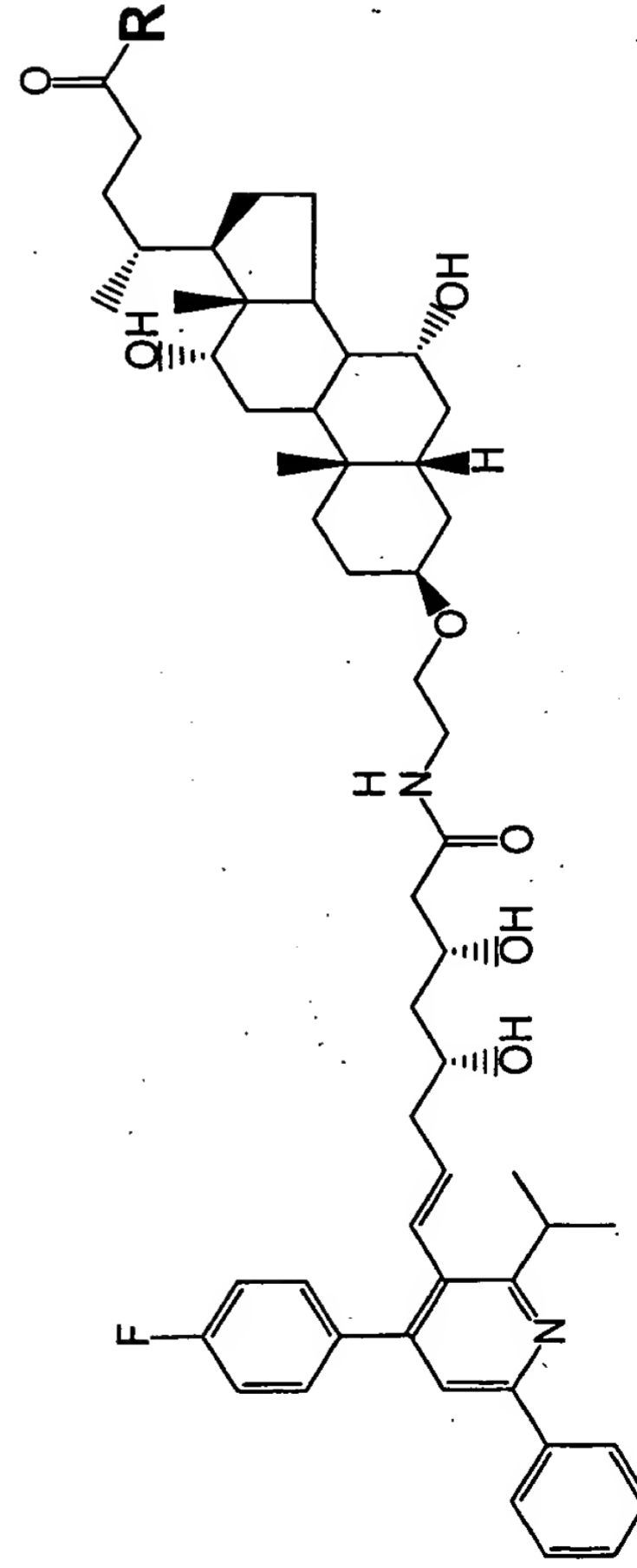


Figure 3

Bile Acid Conjugates of HMG-CoA Reductase Inhibitor



HR 780

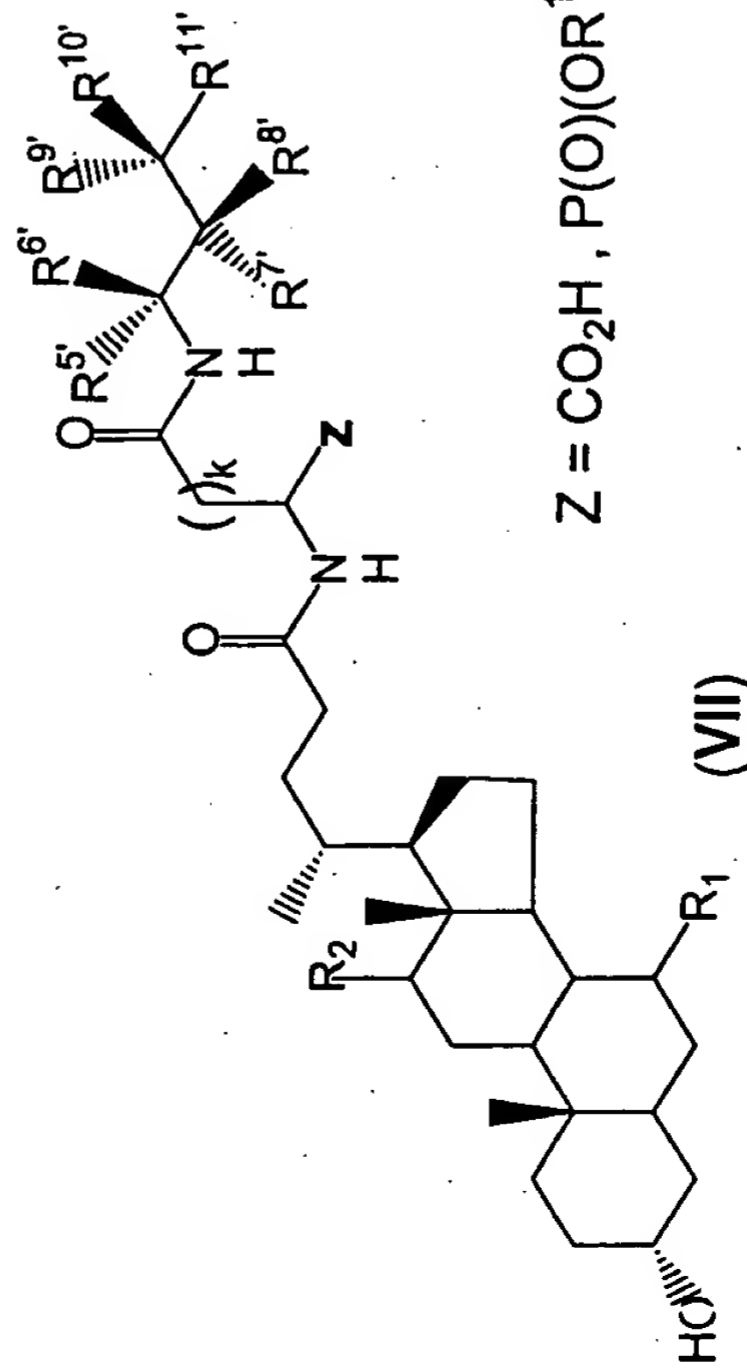
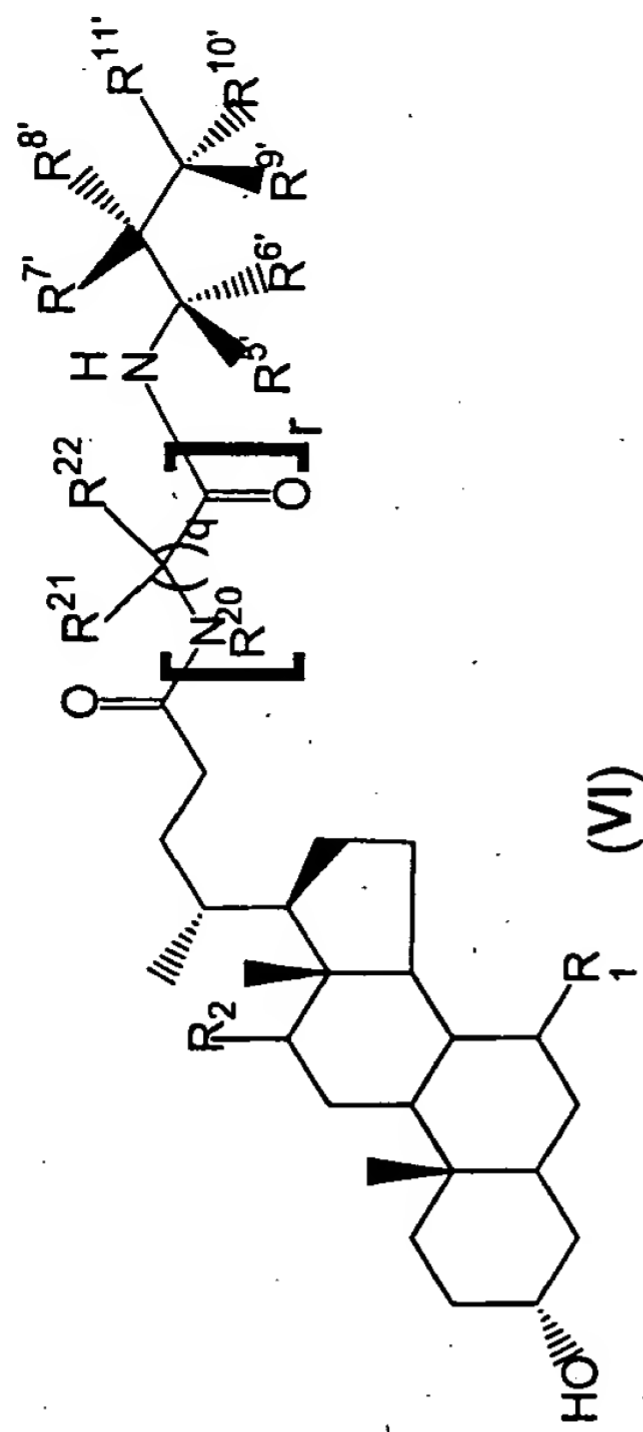
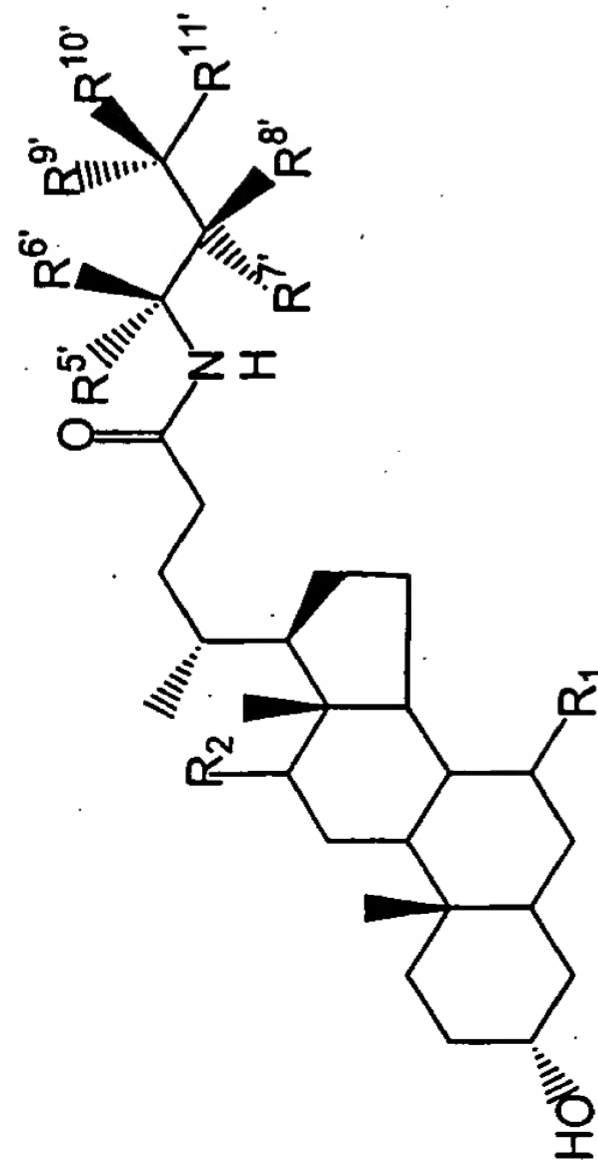


R = OH S 3554

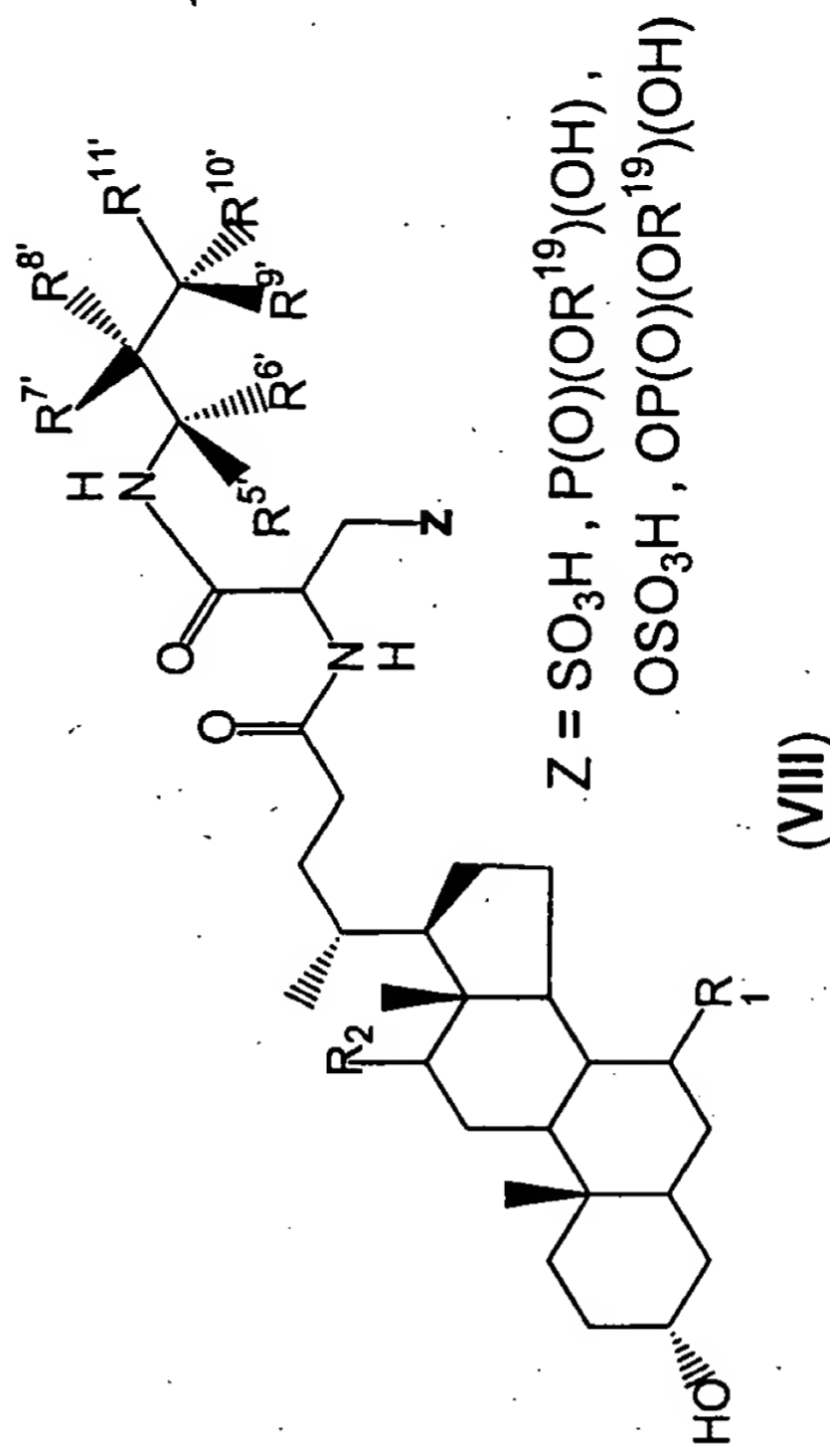
R = NHCH₂CO₂H S 3898

R = NHCH₂CH₂SO₃H S 4193

Figure 4



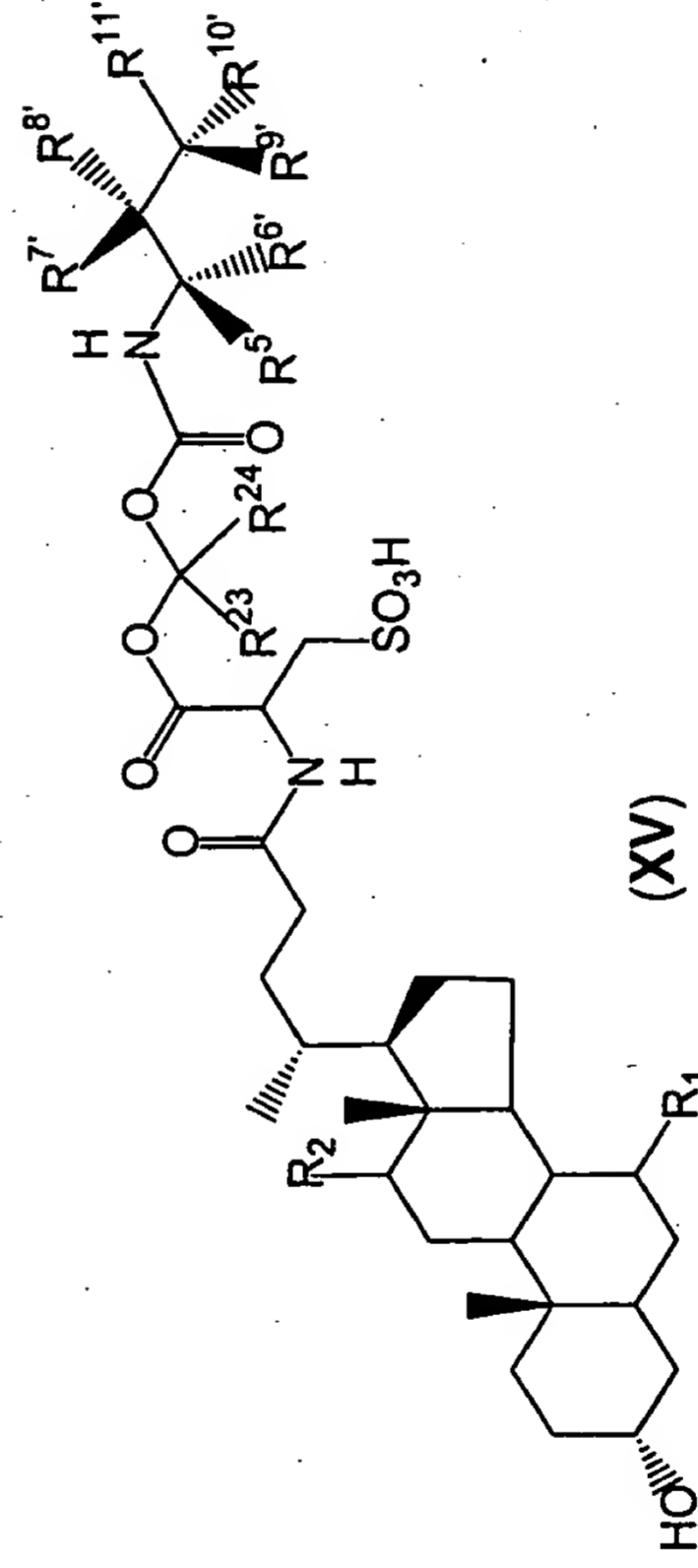
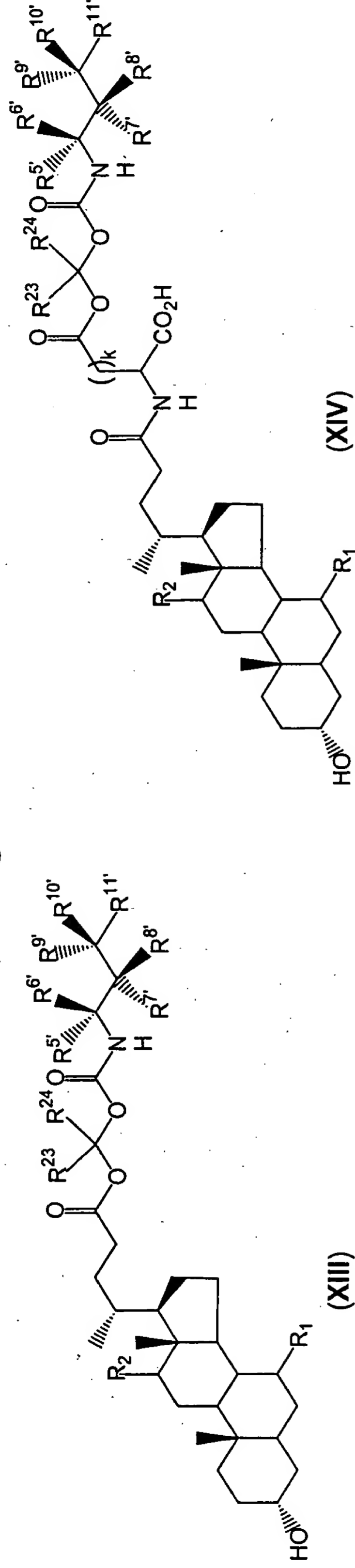
Z = CO₂H, P(O)(OR¹⁹)(OH)



Z = SO₃H, P(O)(OR¹⁹)(OH),
OSO₃H, OP(O)(OR¹⁹)(OH)

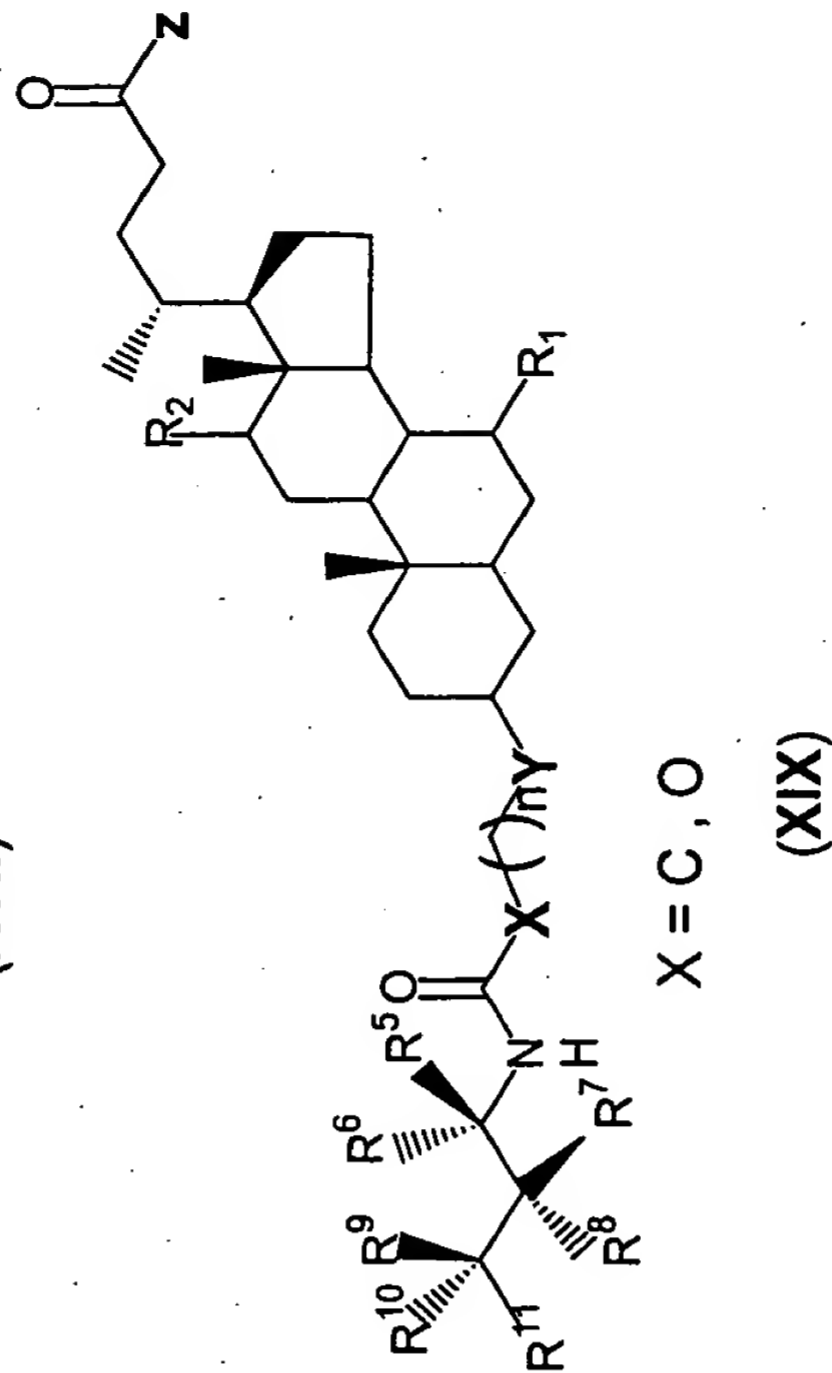
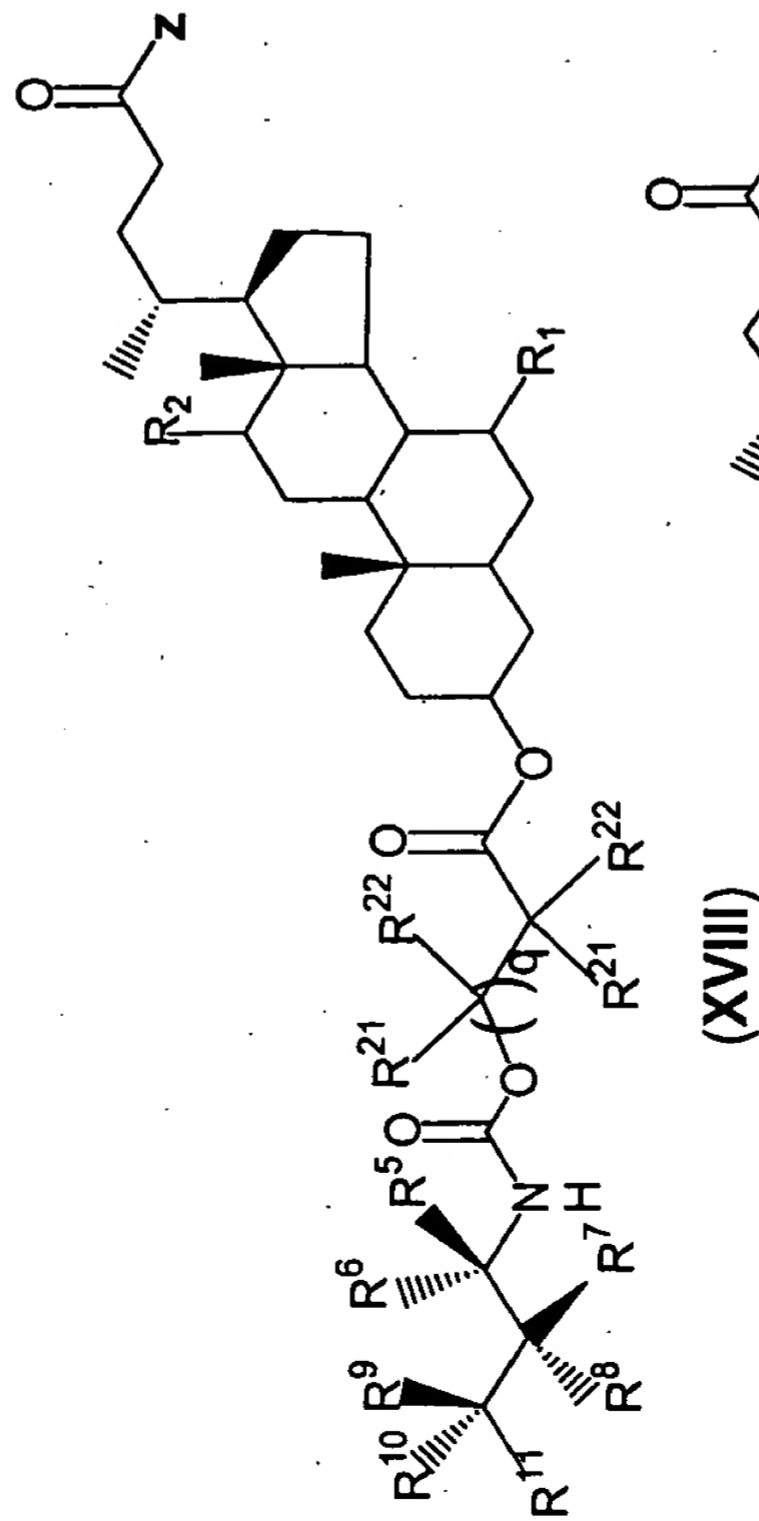
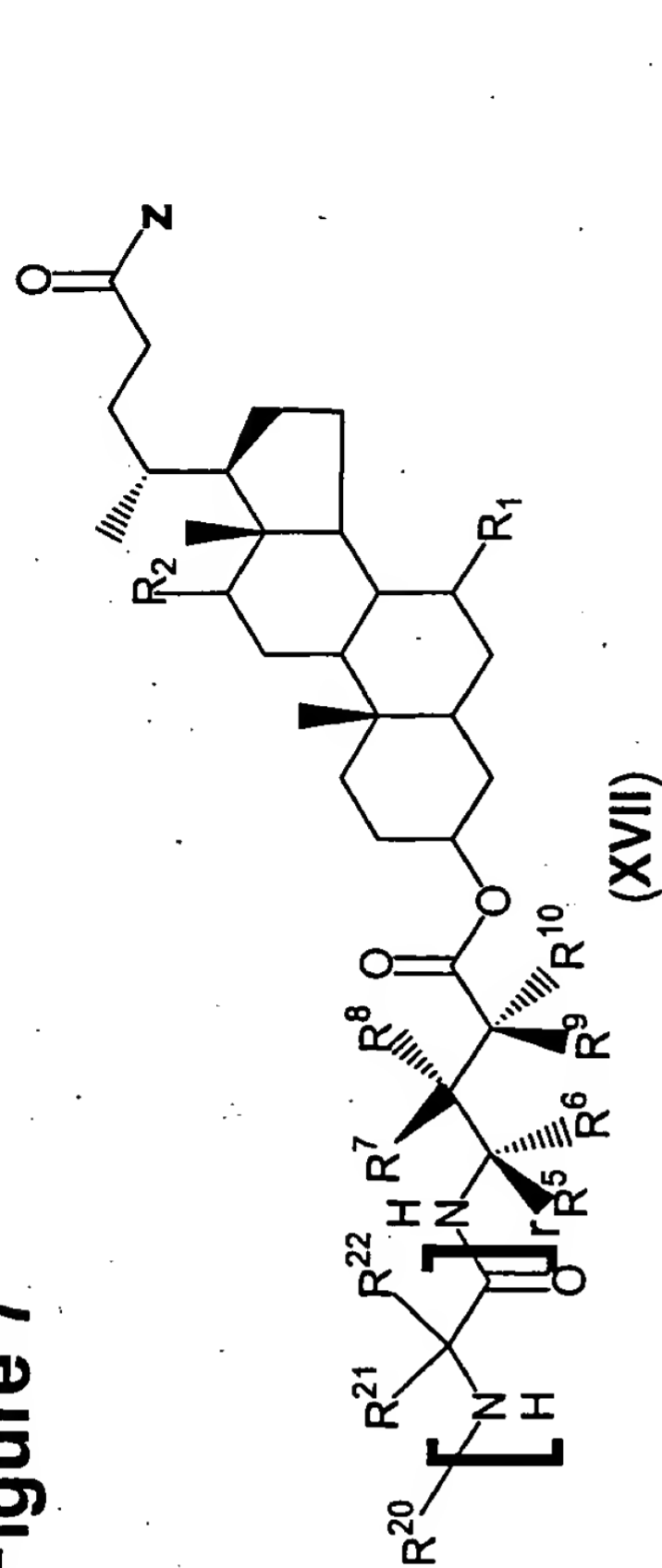
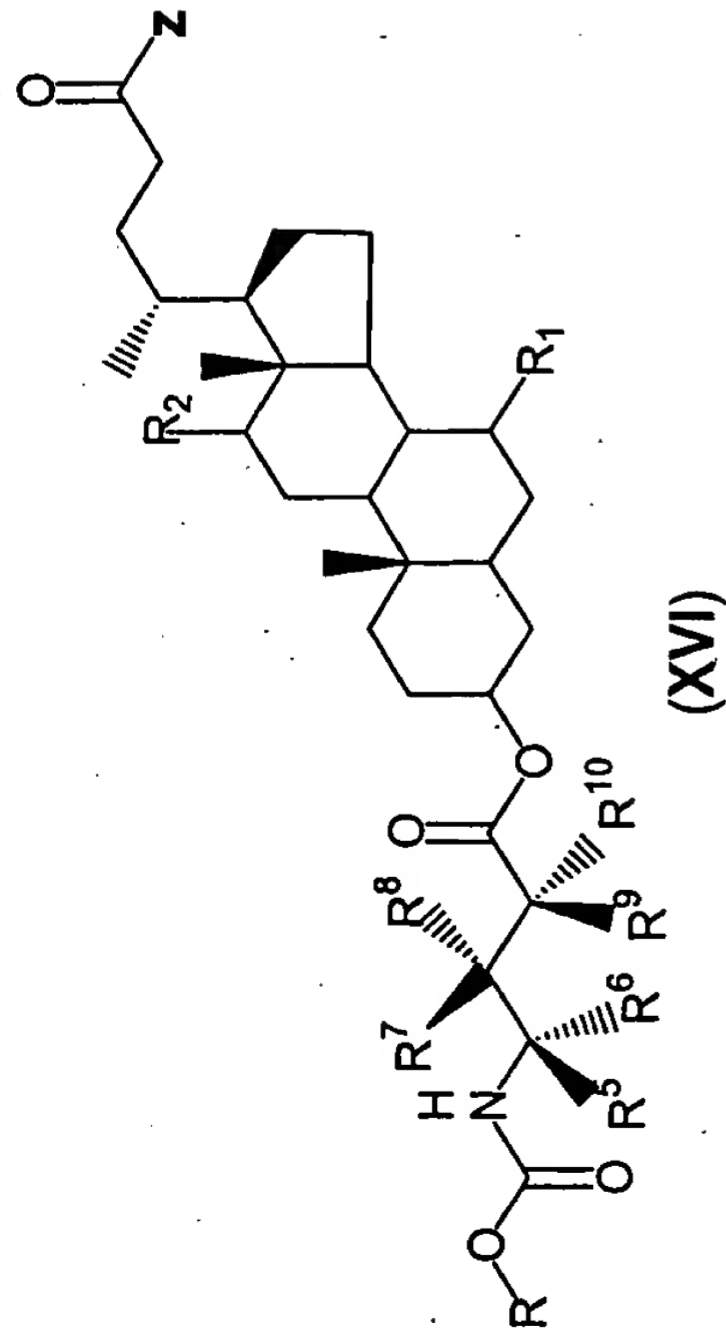
- R1 = α-OH; R2 = α-OH (Cholate)
- R1 = β-OH; R2 = H (Ursodeoxycholate)
- R1 = α-OH; R2 = H (Chenodeoxycholate)
- R1 = H; R2 = α-OH (Deoxycholate)
- R1 = β-OH; R2 = α-OH (Ursocholate)
- R1 = H; R2 = H (Lithocholate)

Figure 6

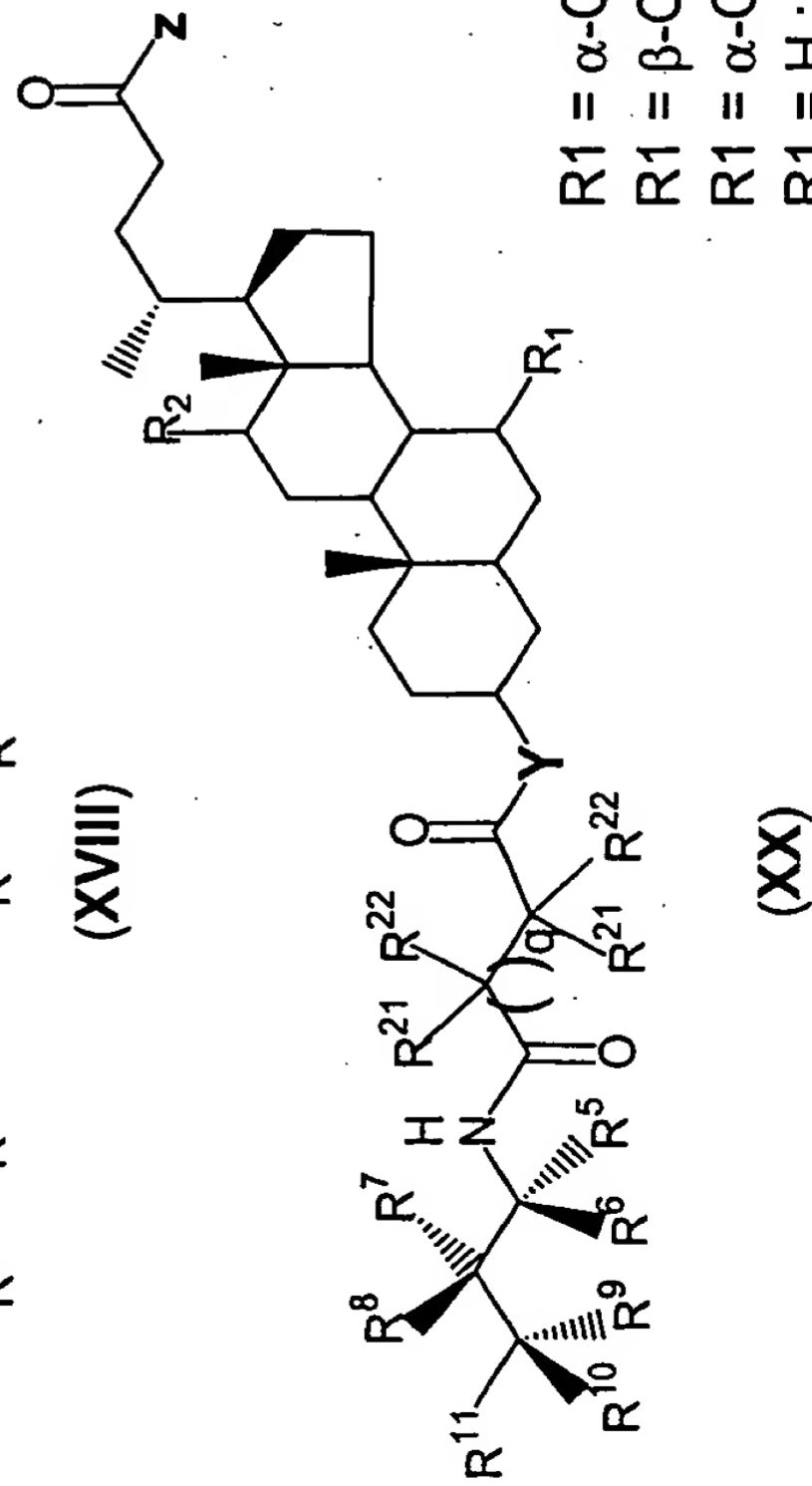


- R1 = α -OH ; R2 = α -OH (Cholate)
- R1 = β -OH ; R2 = H (Ursodeoxycholate)
- R1 = α -OH ; R2 = H (Chenodeoxycholate)
- R1 = H ; R2 = α -OH (Deoxycholate)
- R1 = β -OH ; R2 = α -OH (Ursocholate)
- R1 = H ; R2 = H (Lithocholate)

Figure 7



X = C, O

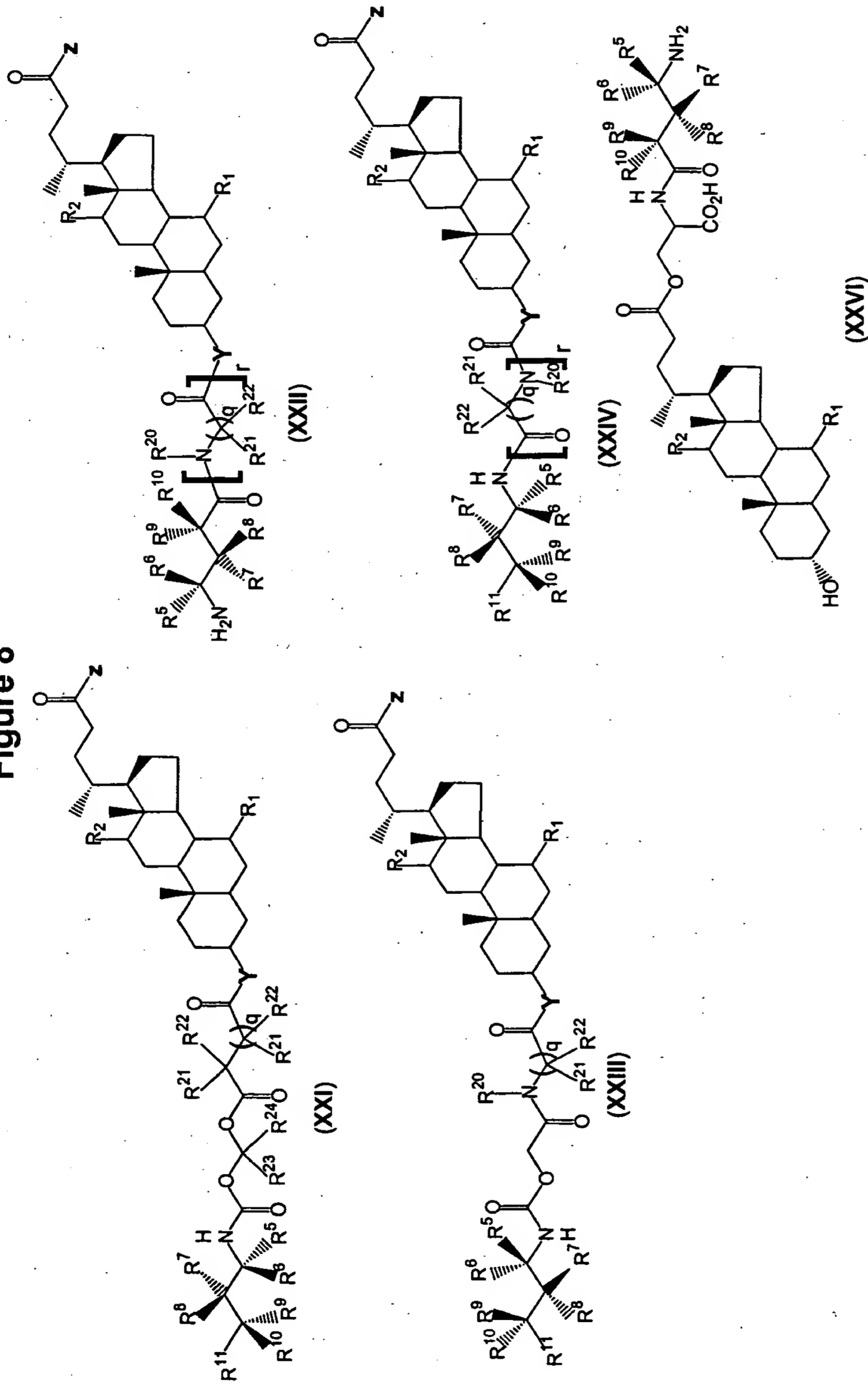


Y = α -O
Y = β -O
Y = α -NH
Y = β -NH

Z = OH
Z = $\text{N} \begin{array}{c} \text{CO}_2\text{H} \\ \text{H} \end{array}$
Z = $\text{N} \begin{array}{c} \text{SO}_3\text{H} \\ \text{H} \end{array}$

R1 = α -OH ; R2 = α -OH (Cholate)
R1 = β -OH ; R2 = H (Ursodeoxycholate)
R1 = α -OH ; R2 = H (Chenodeoxycholate)
R1 = H ; R2 = α -OH (Deoxycholate)
R1 = β -OH ; R2 = α -OH (Ursocholate)
R1 = H ; R2 = H (Lithocholate)

Figure 8

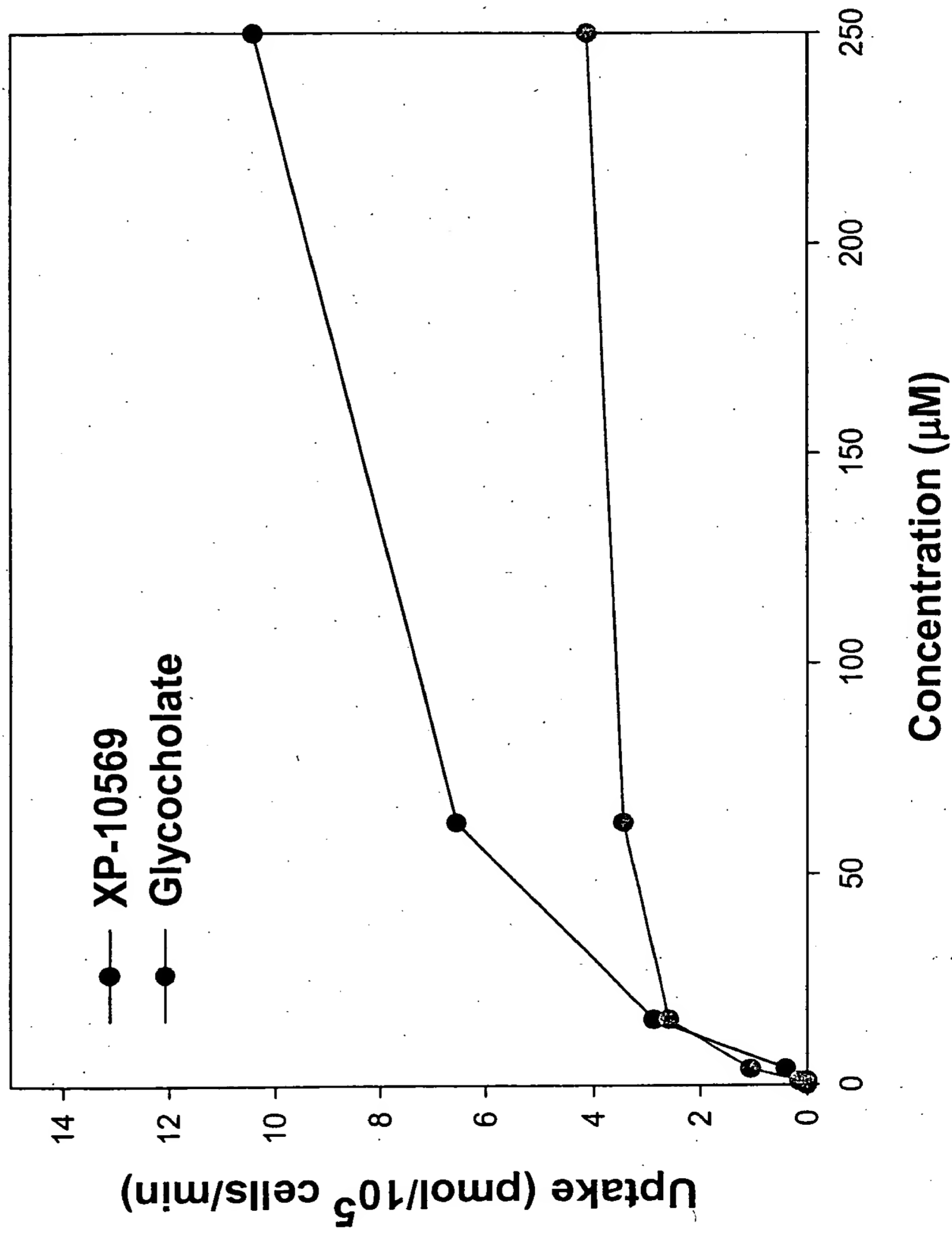


$R_1 = \alpha\text{-OH}$; $R_2 = \alpha\text{-OH}$ (Cholate)
 $R_1 = \beta\text{-OH}$; $R_2 = \text{H}$ (Ursodeoxycholate)
 $R_1 = \alpha\text{-OH}$; $R_2 = \text{H}$ (Chenodeoxycholate)
 $R_1 = \text{H}$; $R_2 = \alpha\text{-OH}$ (Deoxycholate)
 $R_1 = \beta\text{-OH}$; $R_2 = \alpha\text{-OH}$ (Ursocholate)
 $R_1 = \text{H}$; $R_2 = \text{H}$ (Lithocholate)

$Y = \alpha\text{-O}$
 $Y = \beta\text{-O}$
 $Y = \alpha\text{-NH}$
 $Y = \beta\text{-NH}$

$Z = \text{OH}$
 $Z = \text{N} \begin{array}{c} \text{CO}_2\text{H} \\ \text{H} \end{array}$
 $Z = \text{N} \begin{array}{c} \text{SO}_3\text{H} \\ \text{H} \end{array}$

Figure 9: Uptake of (8) (XP10569) or Glycochoholate by IBAT-Transfected CHO Cells



**Figure 10: Uptake of (8) (XP10569) or Glycocholate by
LBAT-Transfected CHO Cells**

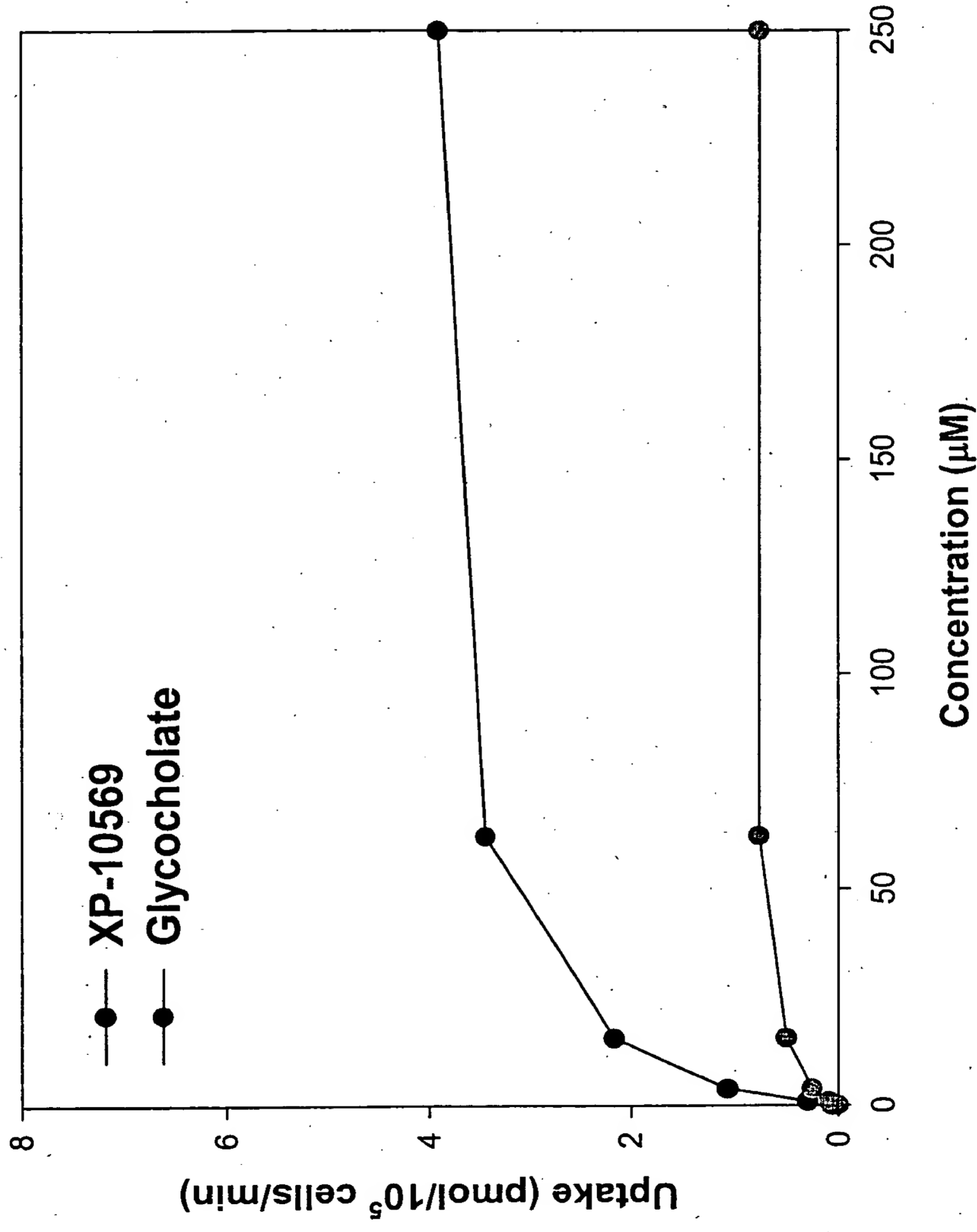


Figure 11

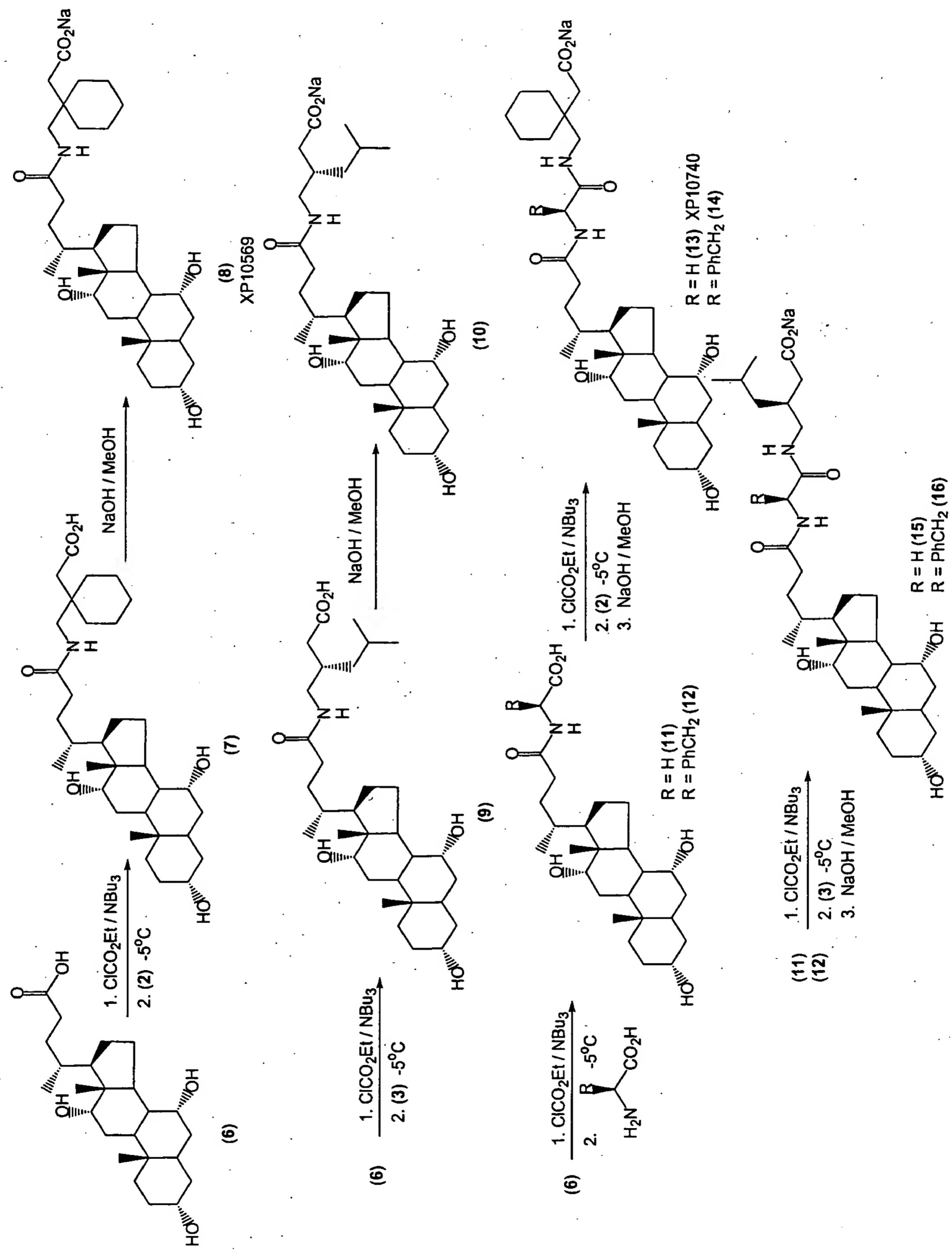


Figure 12

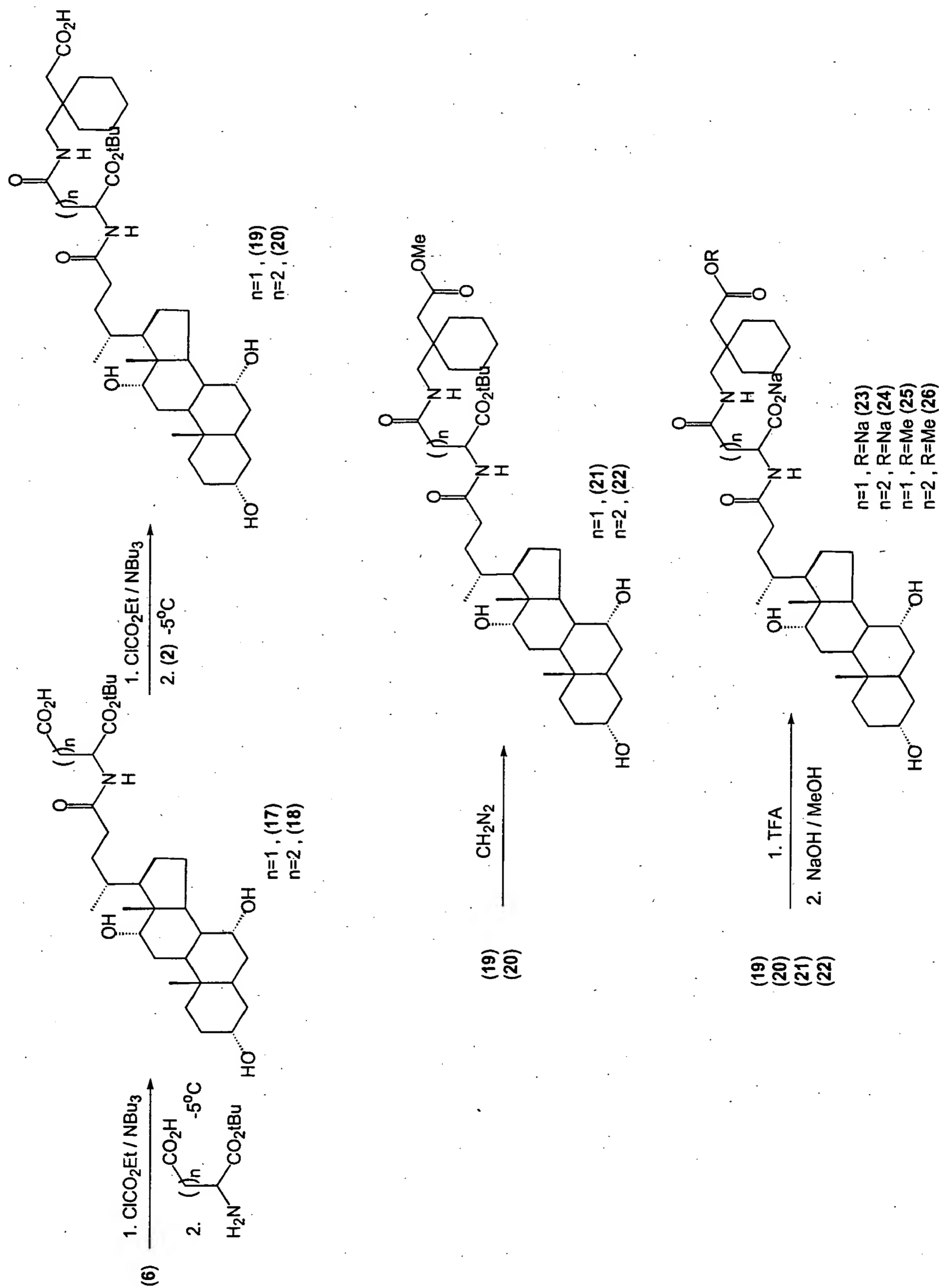


Figure 13

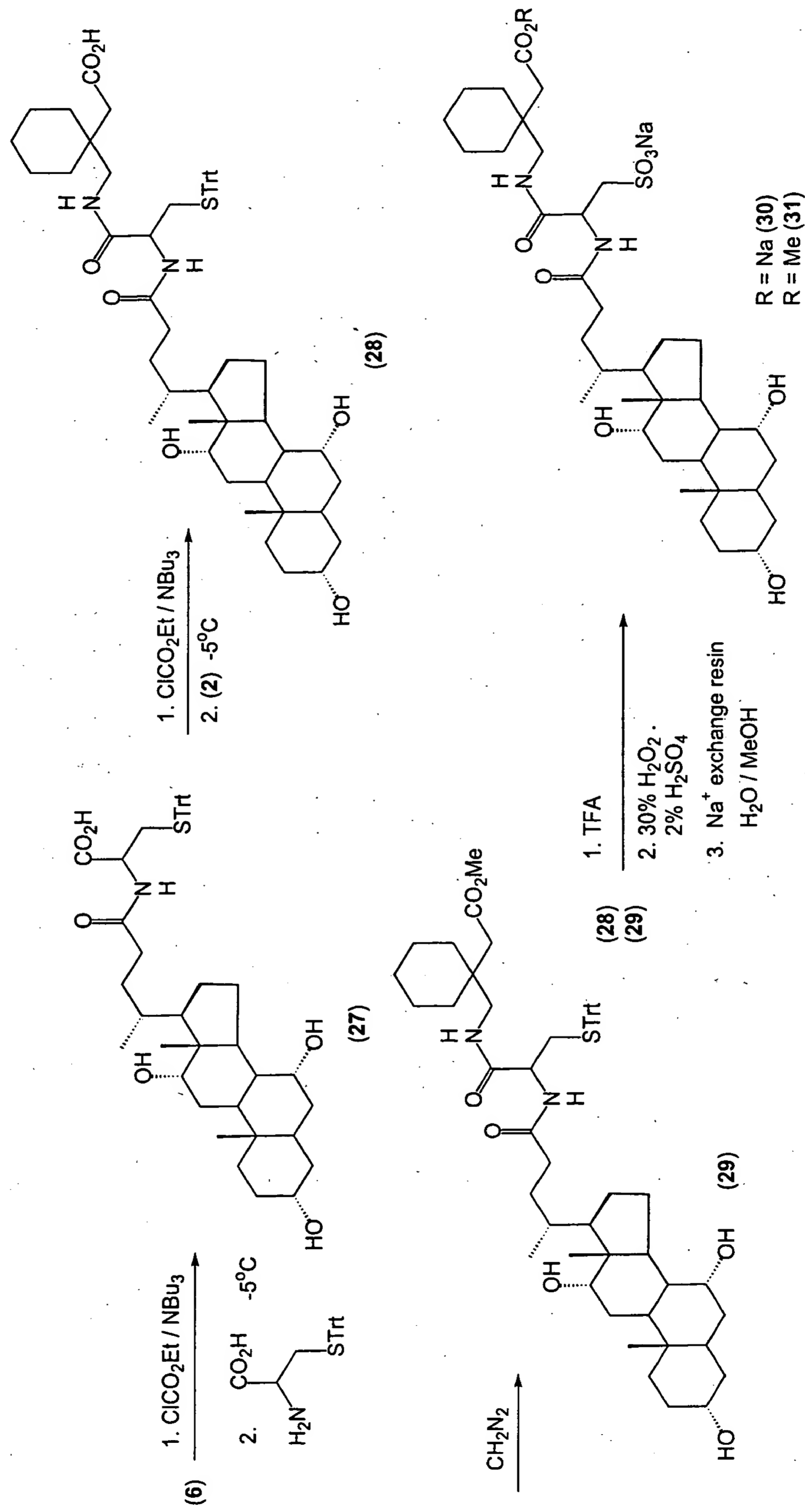


Figure 14

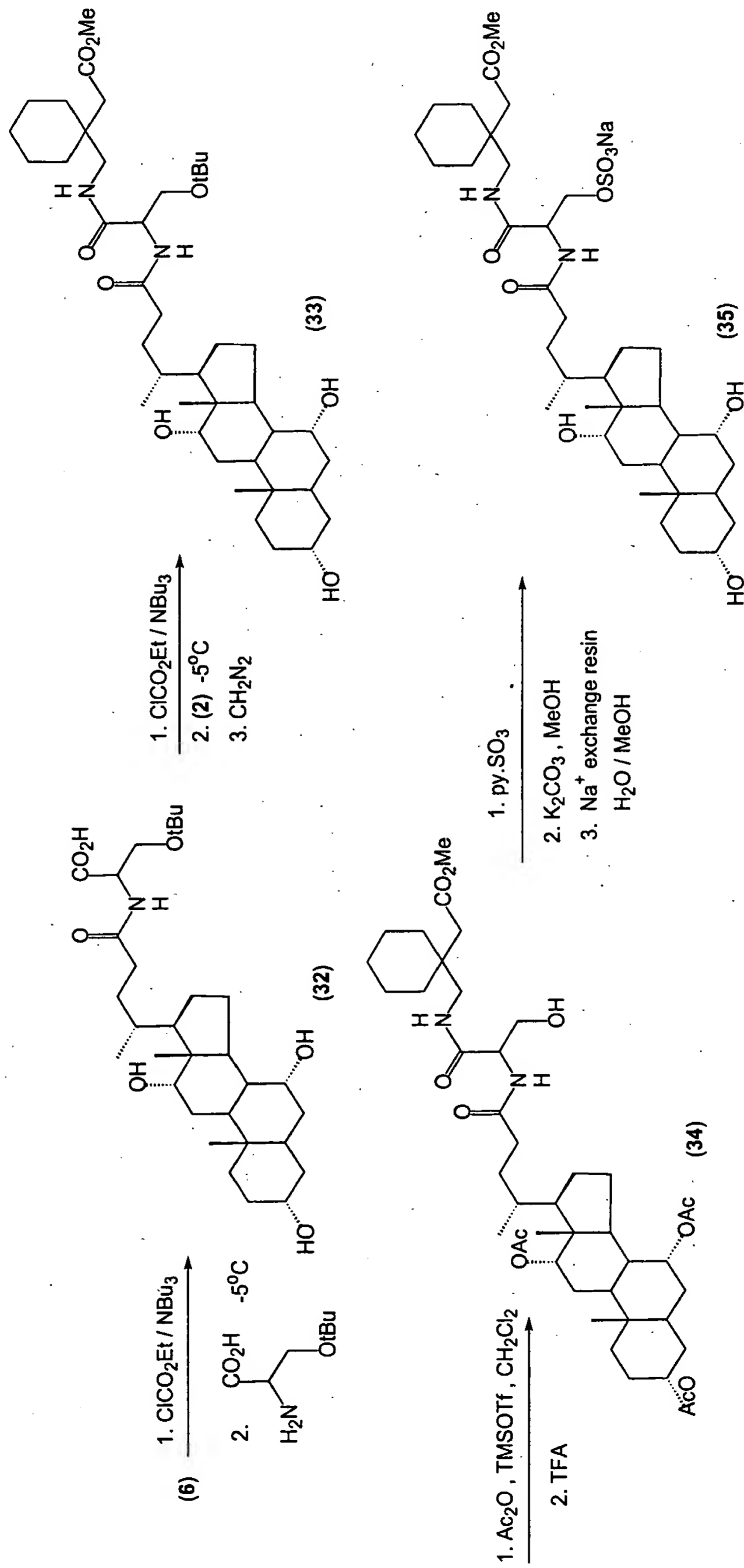


Figure 15

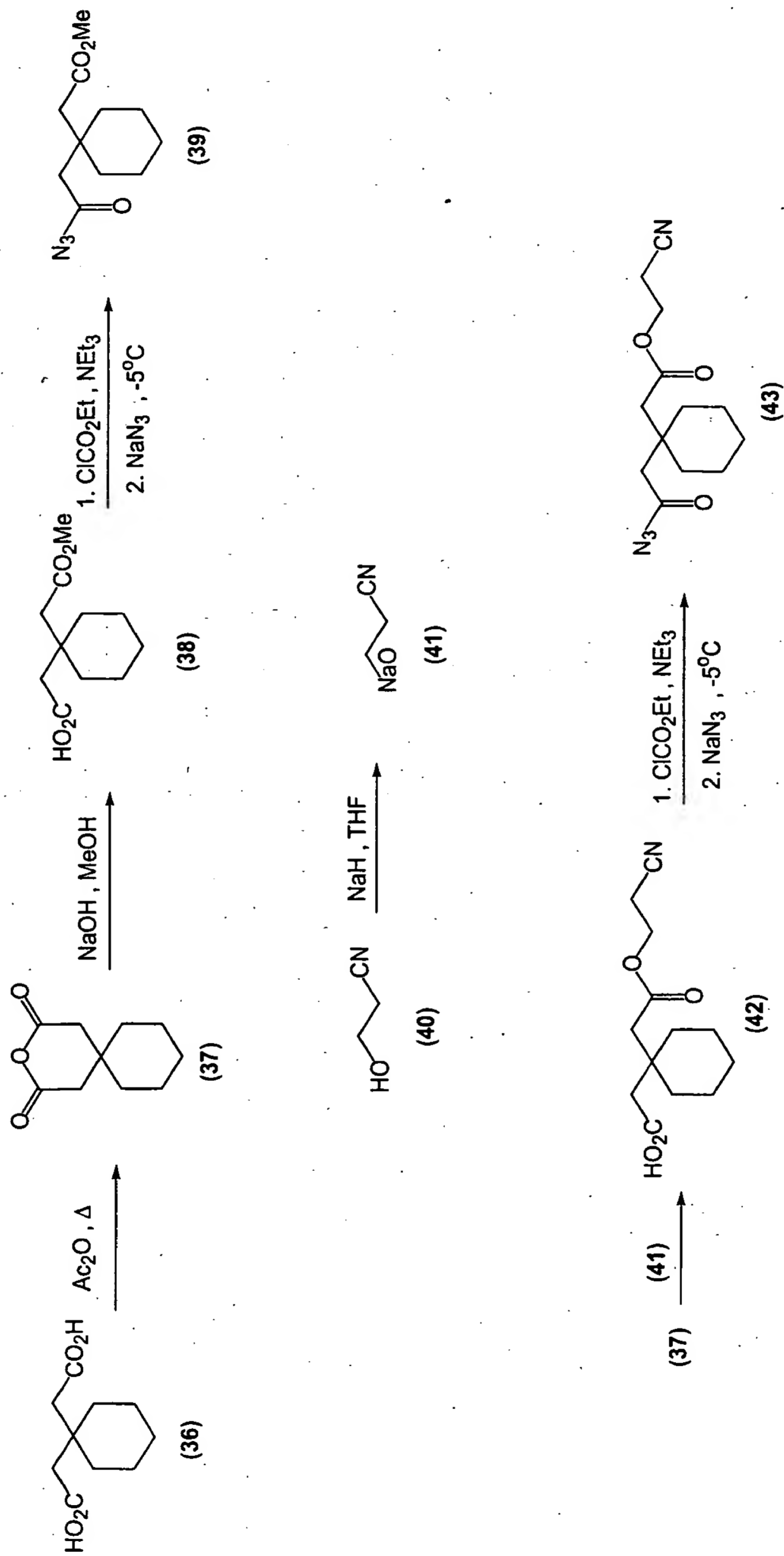


Figure 16

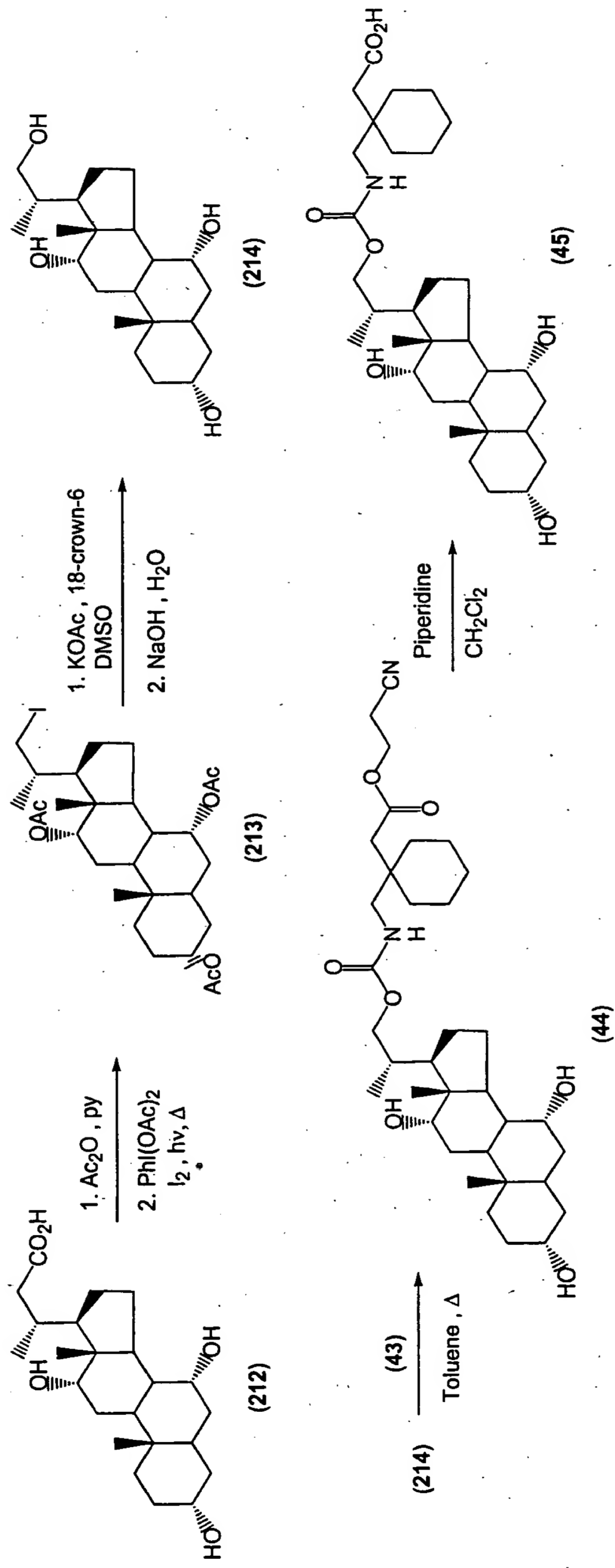


Figure 17

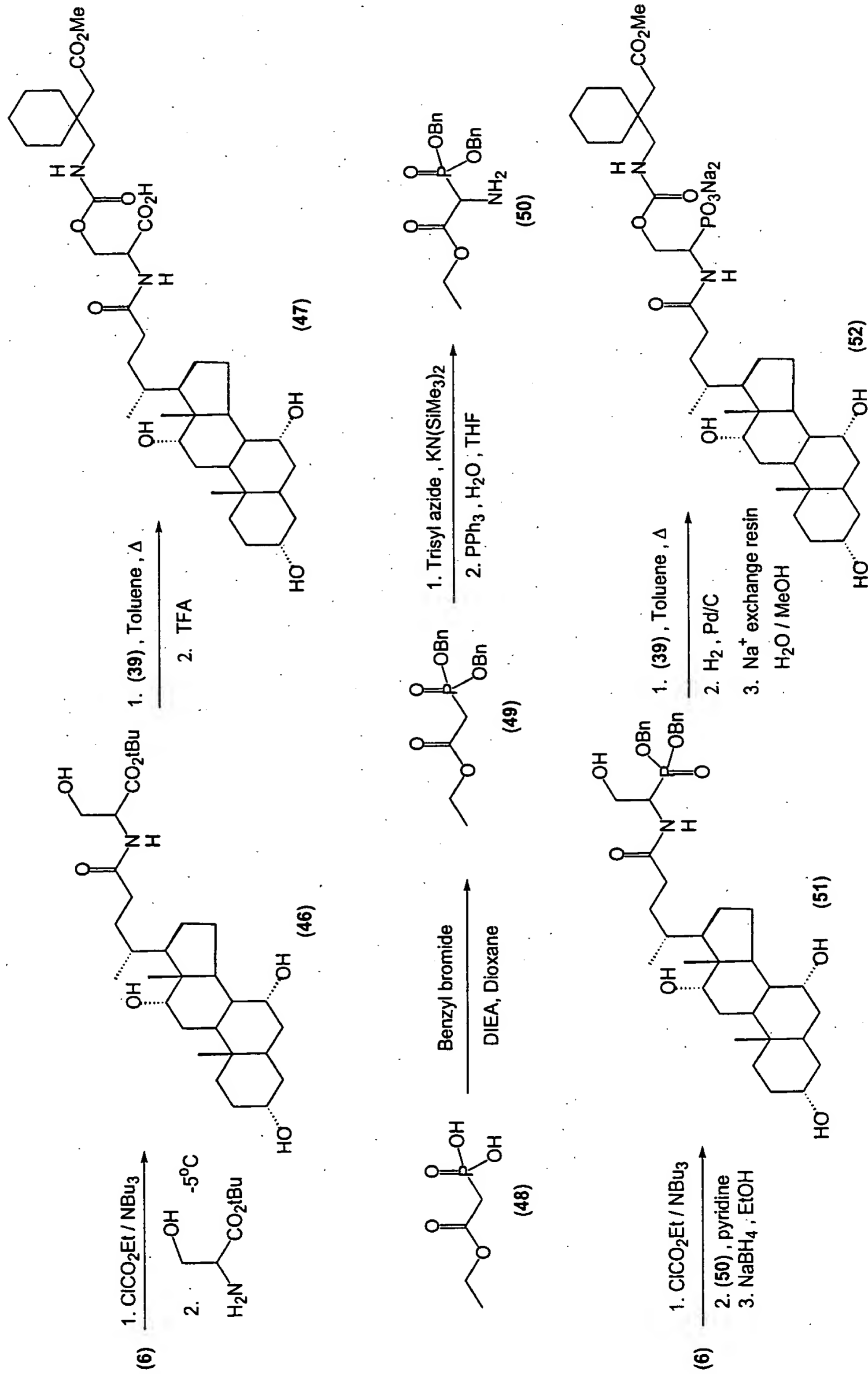


Figure 19

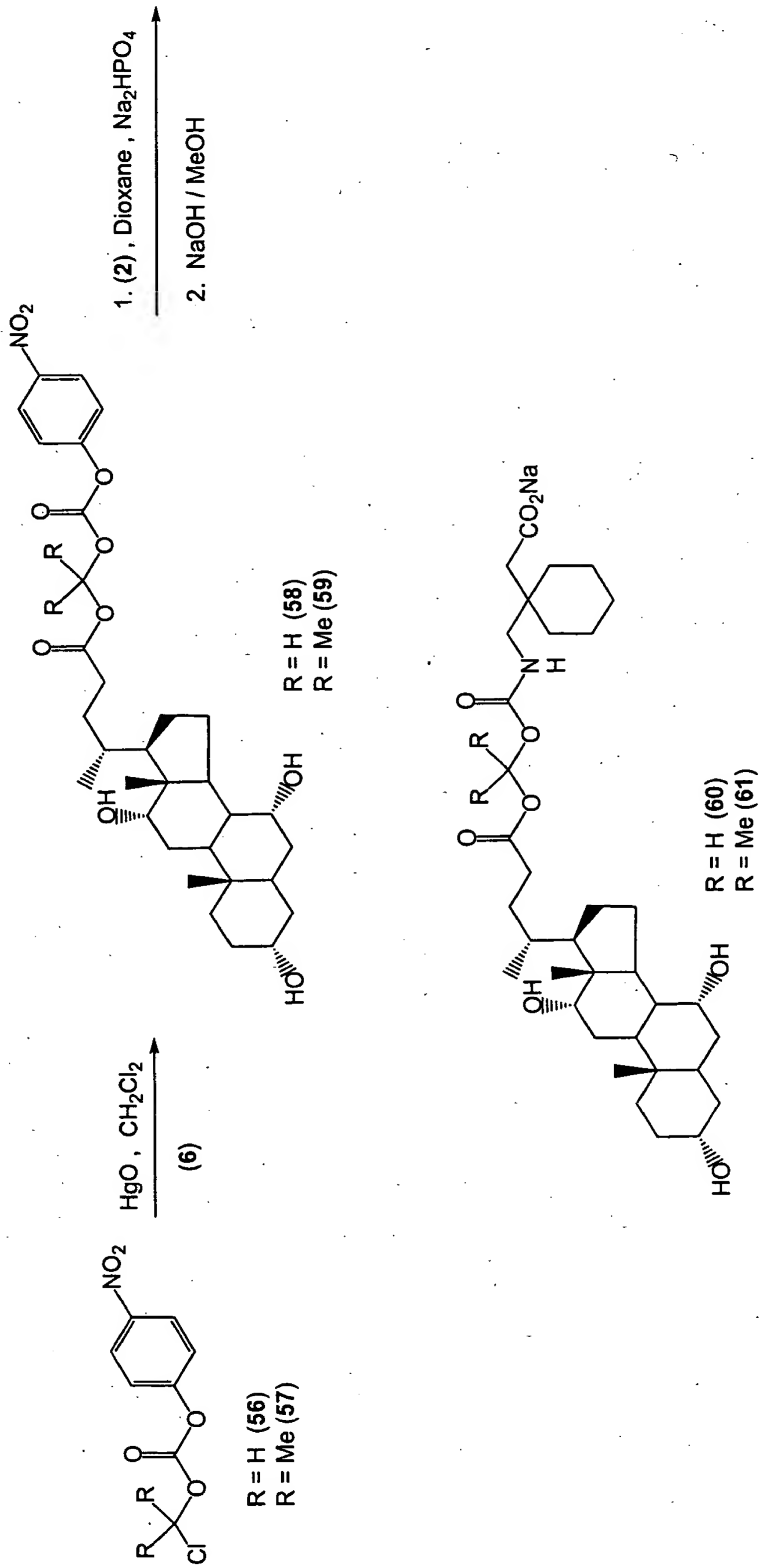
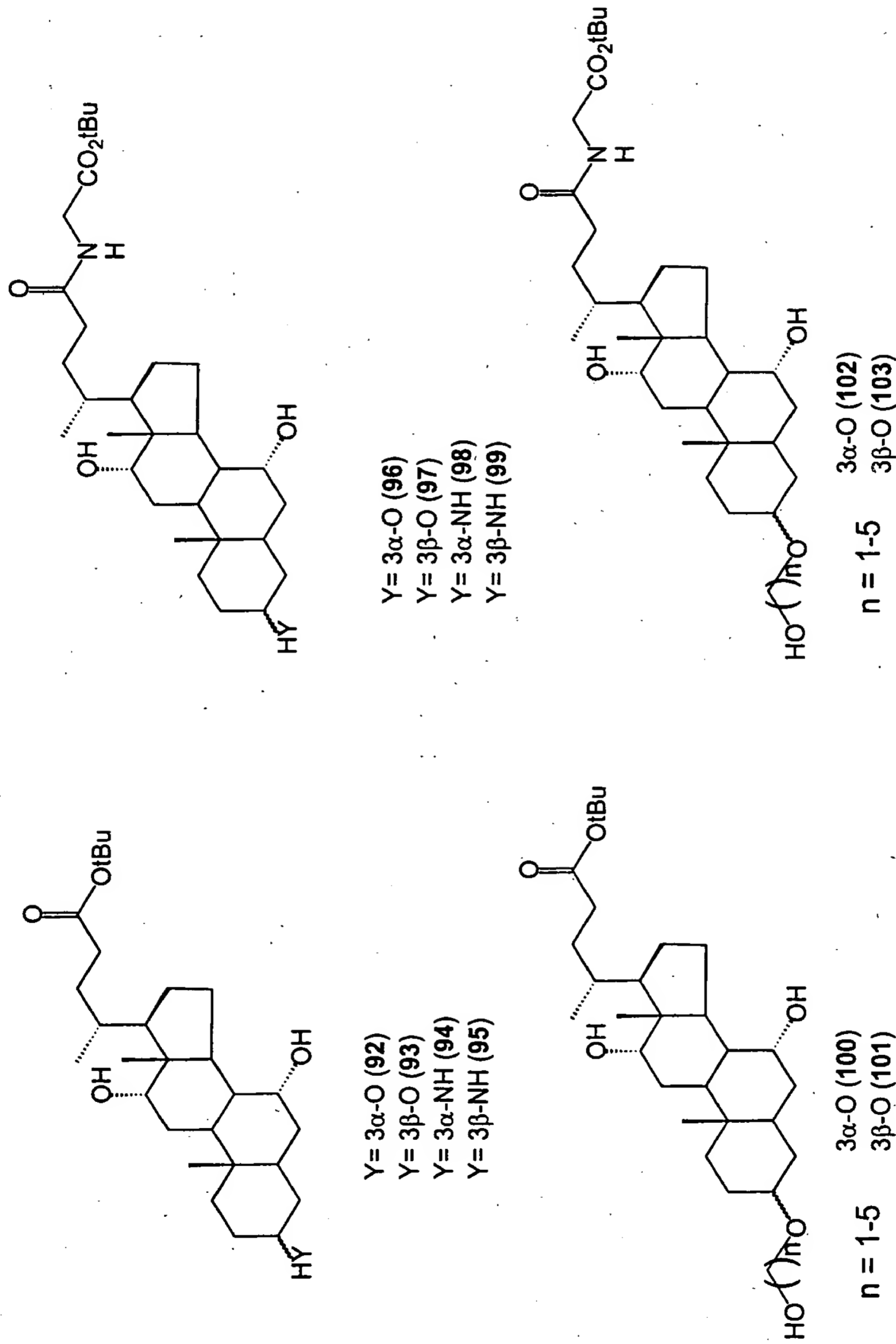


Figure 22



Compounds (92) - (103) prepared following methods described in co-pending application "Bile Acid-Derived Compounds for Enhancing Oral Absorption and Systemic Bioavailability of Drugs" assigned to XenoPort, Inc.

Figure 24

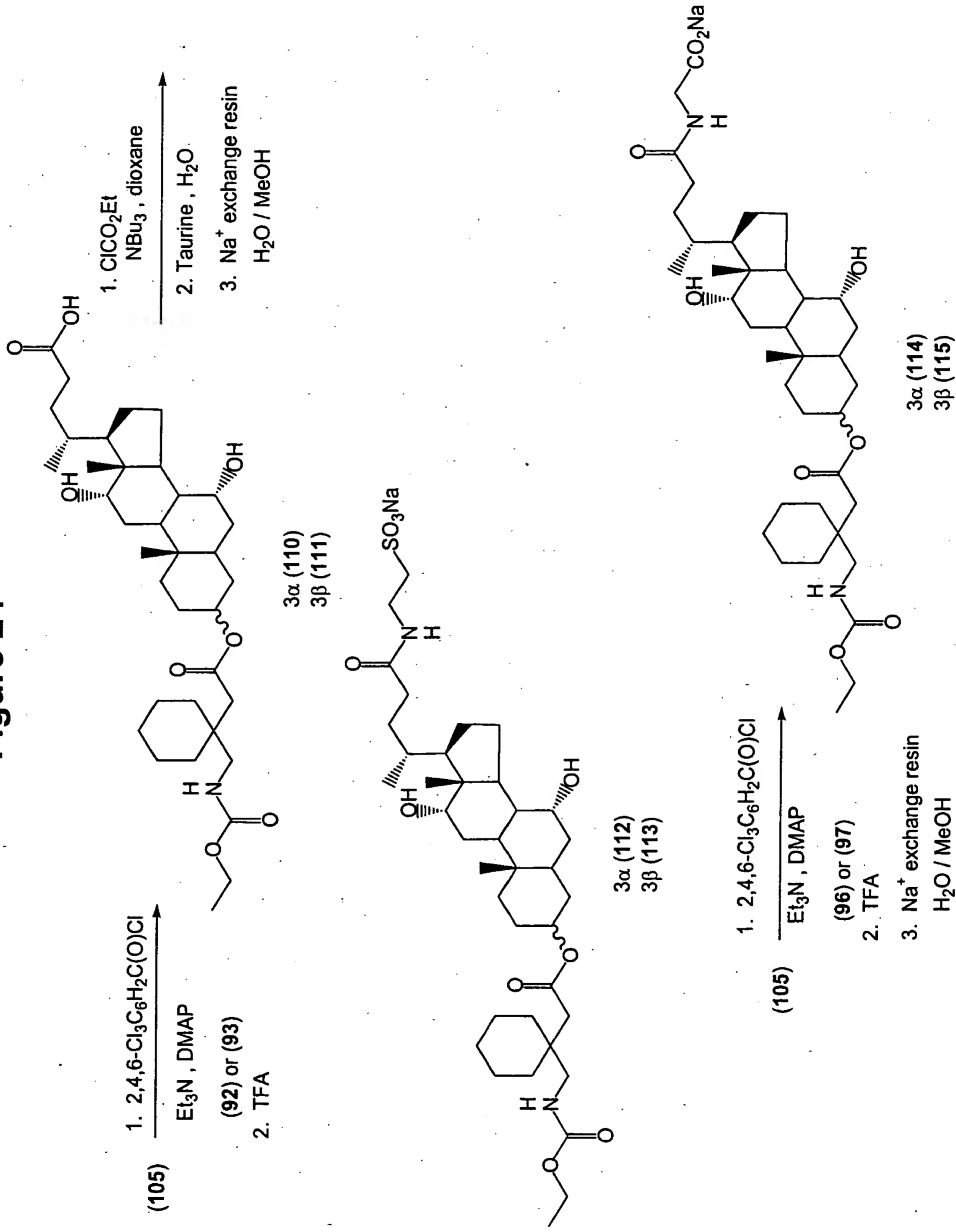


Figure 25

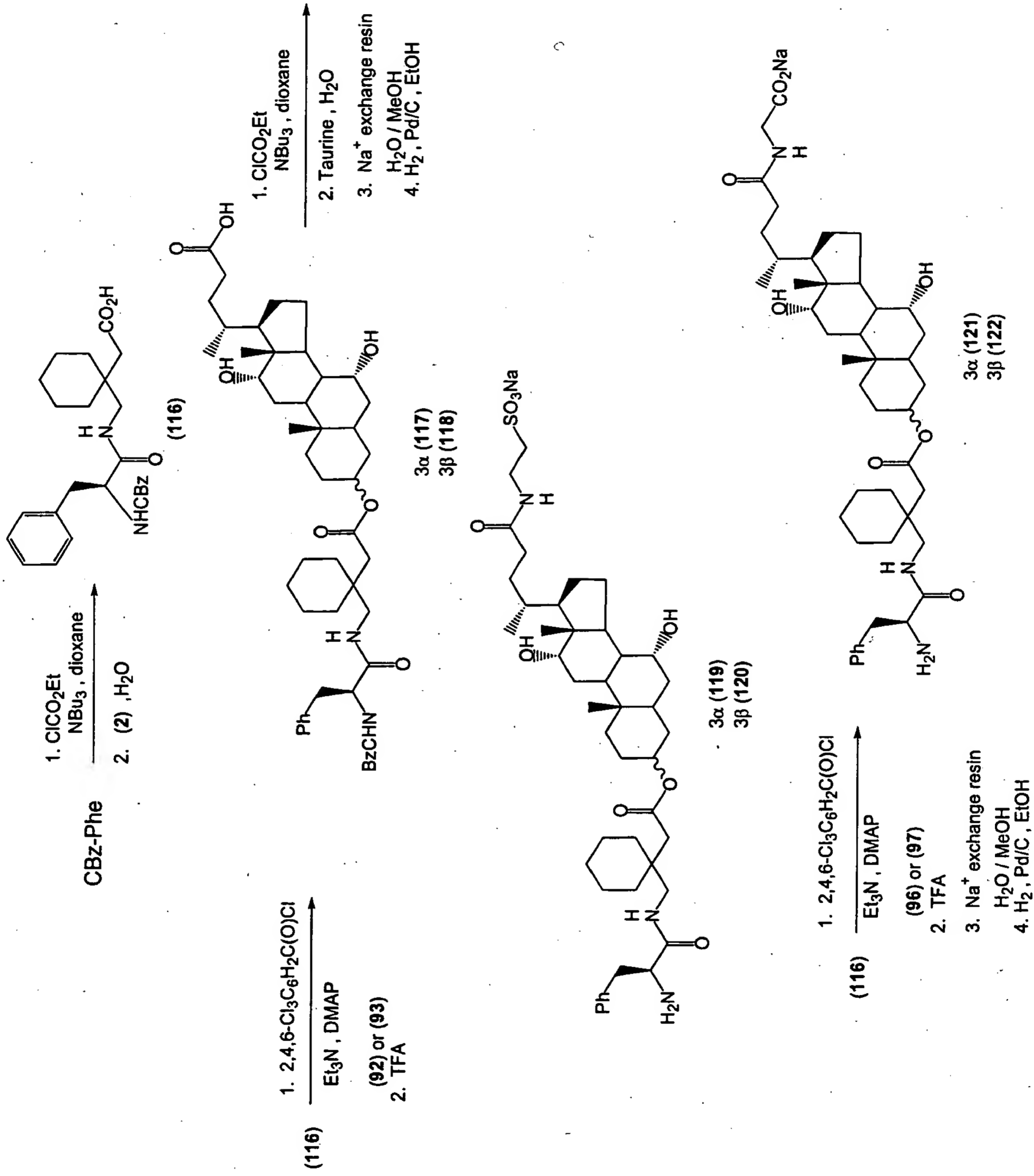


Figure 27

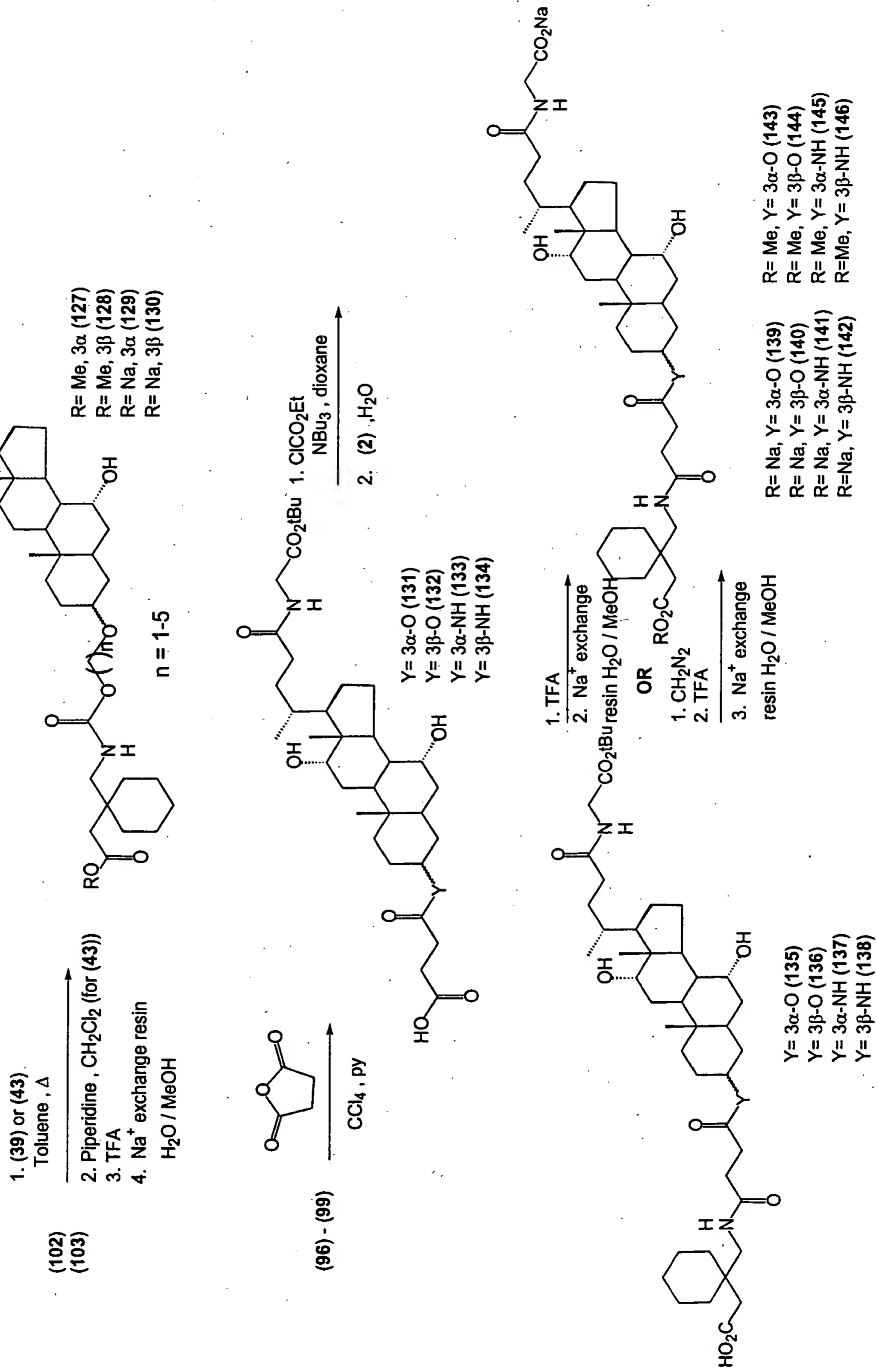


Figure 28

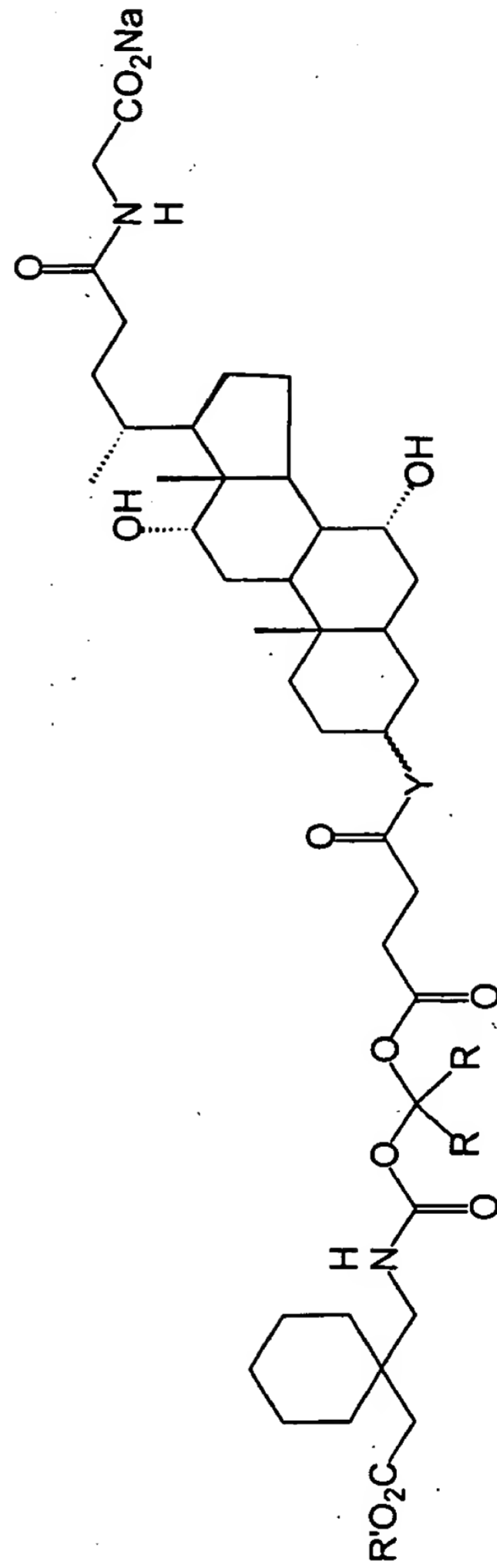
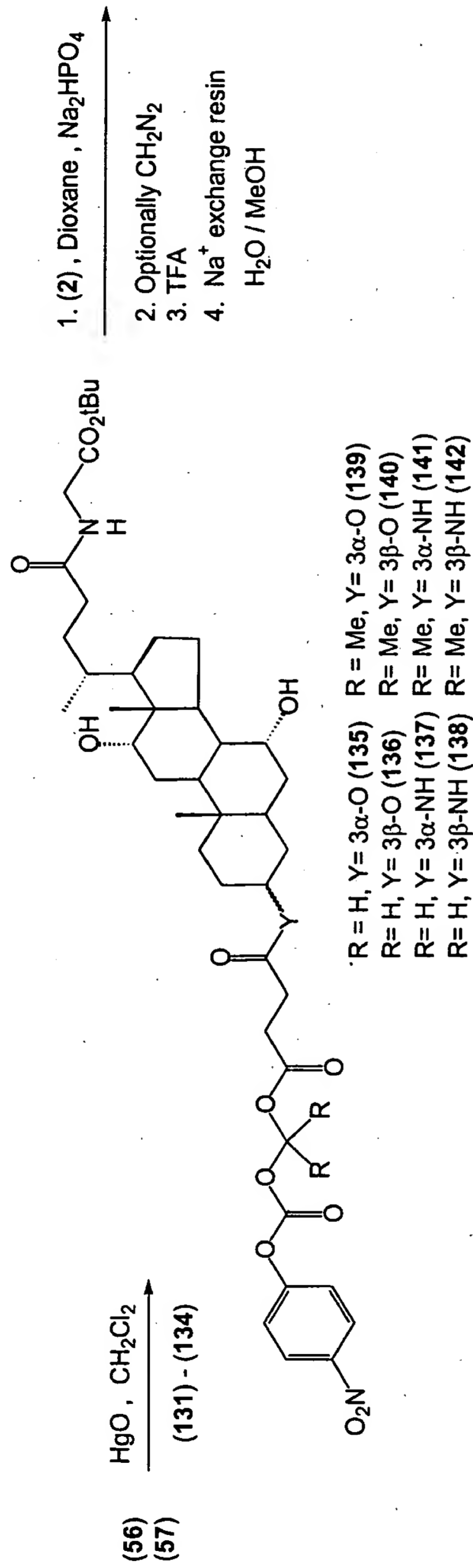


Figure 29

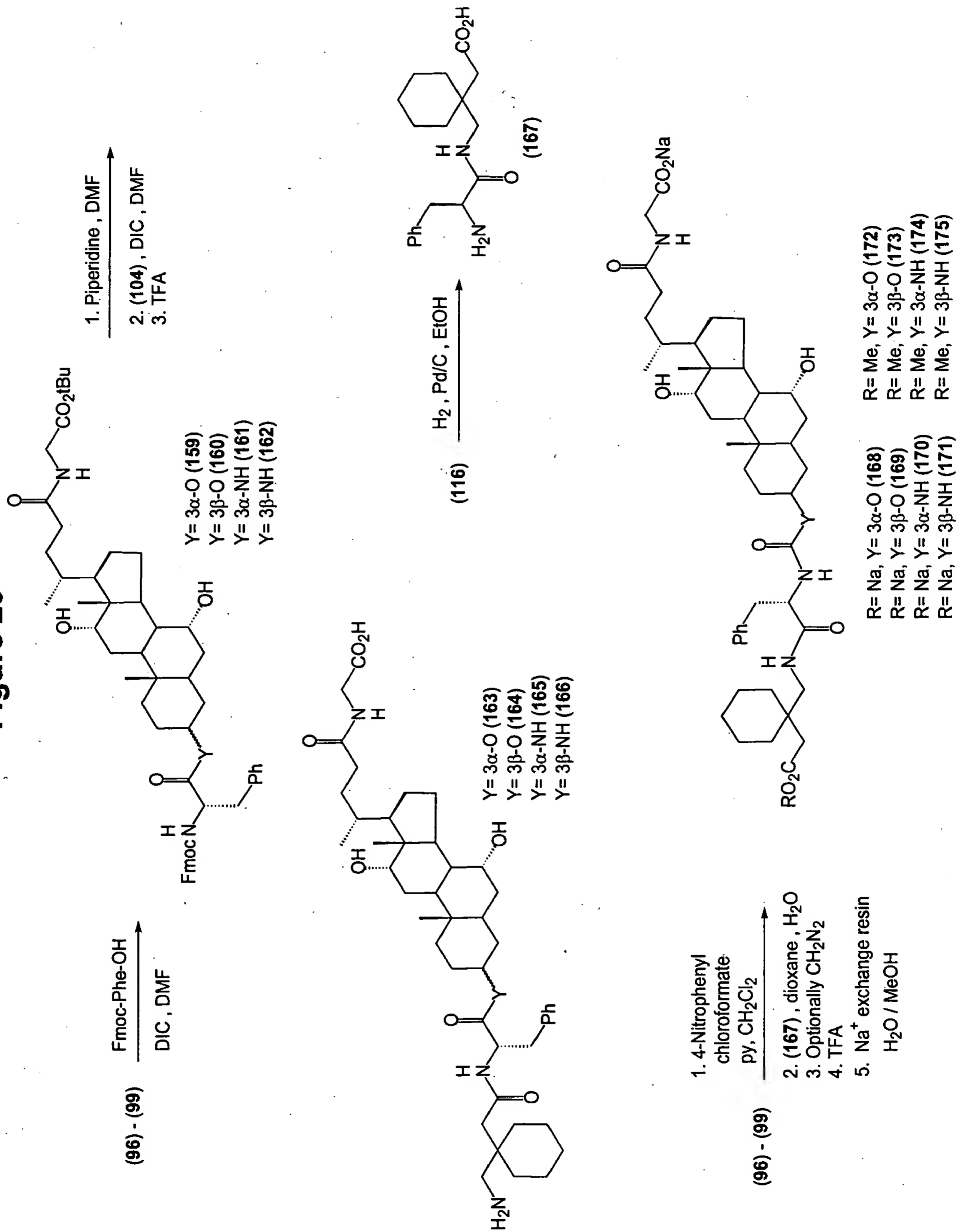


Figure 30

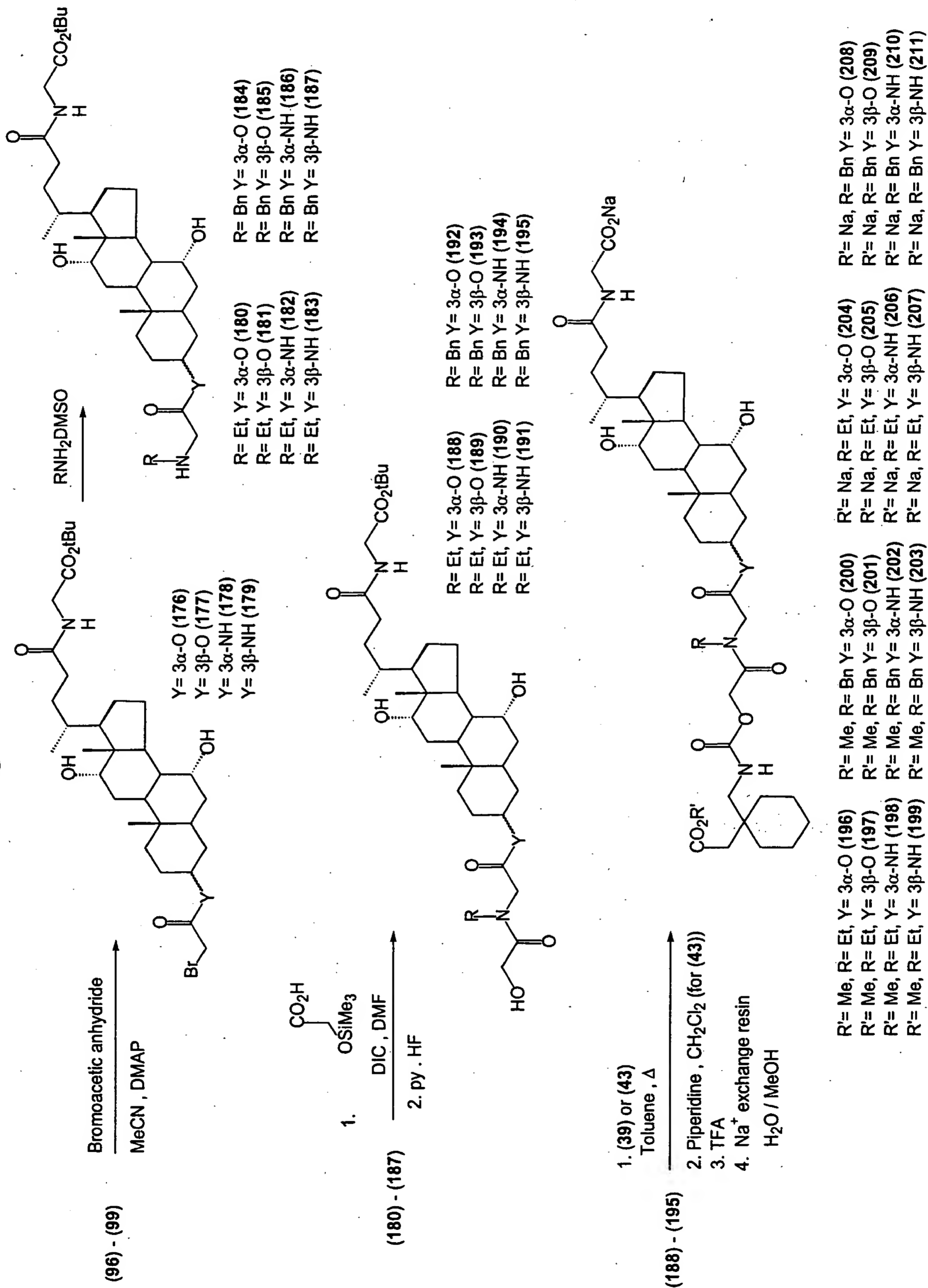
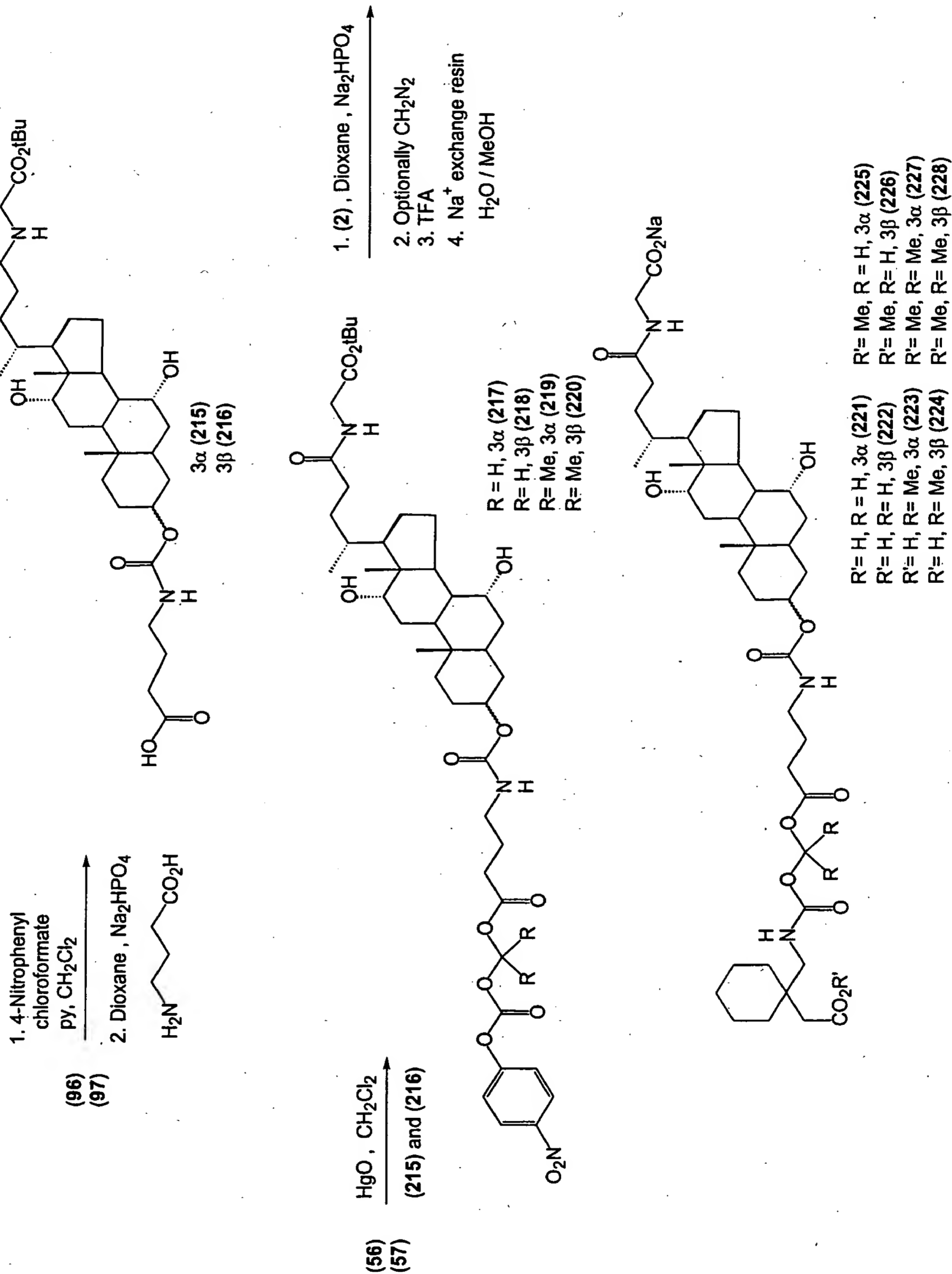


Figure 31



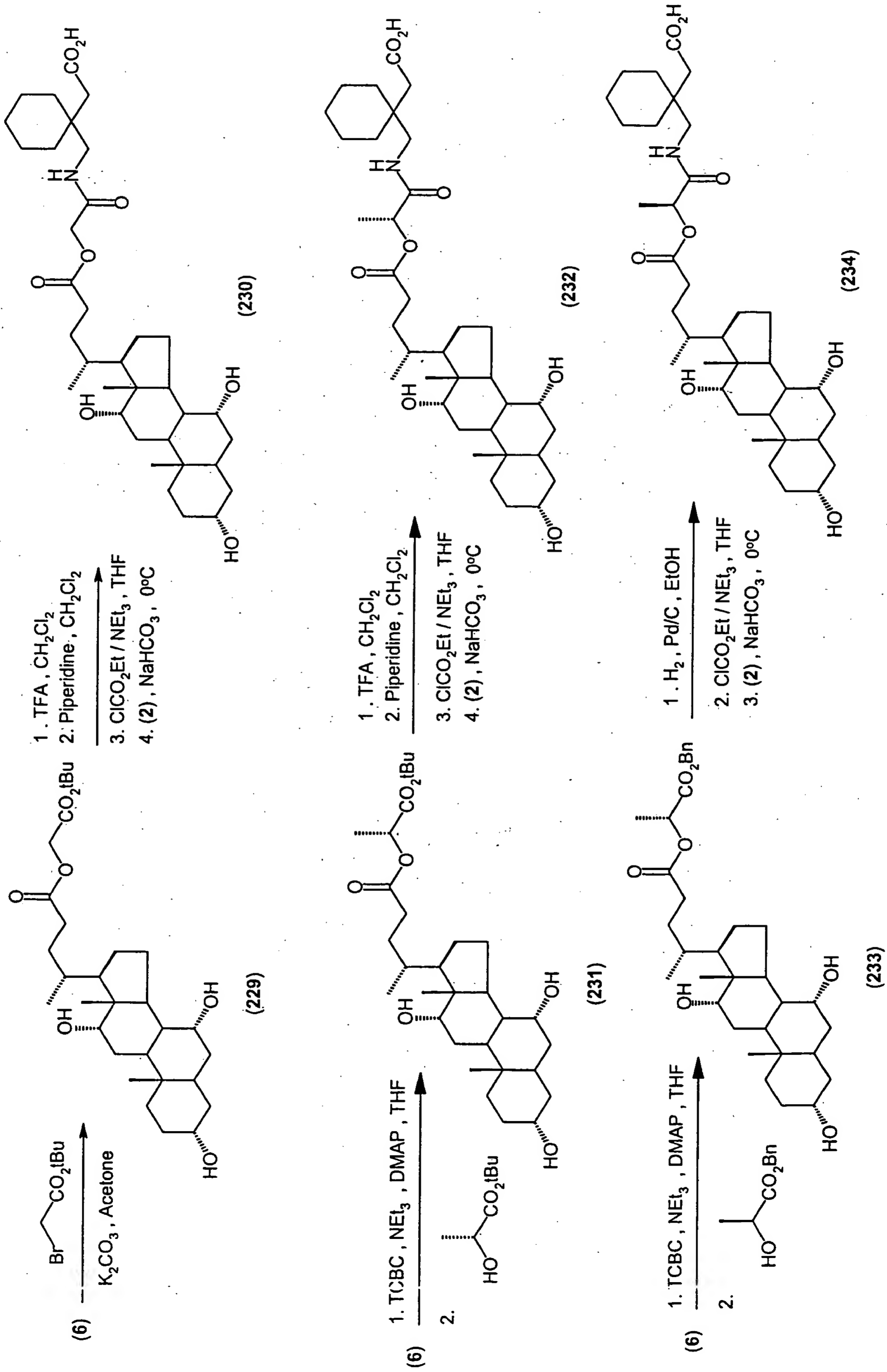


Figure 33

